

Some of these have been described as being reddish gray, others pinkish, and some yellowish white

The necrosis of the valve, it would seem, advanced with actual liquefaction, and may be so extensive that perforation of the leaflet occurs, and the opening in the leaflet may be plugged by the thrombotic mass

Another feature is the tendency for the process to extend to the adjacent myocardium, and abscess formation with discharge of the abscess content into the blood-stream may result either in the formation of a small cavity in the heart wall or, as in one of these cases reported here, in perforation of the septum. These thrombotic masses upon the valves are heavily infected and are another fertile source for infected emboli. The lesions in the myocardium are chiefly abscesses such as are found in other organs

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CLINIC OF DR HARLOW BROOKS

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THE TREATMENT OF PNEUMONIA

Based on a Broad Clinical Experience and a Description of Measures which One Will Be Called Upon Most Frequently to Use, Knowledge Not Derived from the Laboratory Nor from the Dead-house, but from a Study of the Disease as it is Seen Clinically in the Ward and By the Bedside of the Private Patient

GENTLEMEN At this period of the year the treatment of pneumonia is a very timely and important question There is no standard, routine, or "ward" treatment for pneumonia There is probably no other medical condition in which treatment must be more determined by the individual patient and case than is true of pneumonia The more individualistic the treatment, the more successful its results

It has been stated that the successful treatment of pneumonia is more dependant upon nursing than upon medical skill This is about one-third or, perhaps, one-half the truth As a matter of real fact, successful treatment depends chiefly on the prompt and individualistic application of many well-established medical procedures applied at the correct time, not too soon, not too late, and the more definitely these measures are adapted to the definite case under study, the more successful the result Great versatility, a broad grasp of the whole armamentarium of the well-equipped physician is demanded, and promptness of action, decisive procedures are often required On the other hand, a lack of meddling therapeutics, a letting of the patient be, is perhaps even more needed at times

We shall have very little to say of the specific treatment of pneumonia today As yet this is a very definitely limited

and circumscribed field, but I believe that your generation, certainly that which is to follow you, will have put in its hands a weapon perhaps as effective in pneumonia as antitoxin is in diphtheria or mercury in syphilis. That time has not yet arrived, and in our talk today I shall merely attempt to give you, as it were, the general consensus of therapeutic opinion of the present-day generation of practitioners. I shall have little to say of theories, of hopes for the future. I shall try to point out to you, in so far as a broad clinical experience with this terrible disease has schooled me, those measures which you will be most frequently called upon to use. This knowledge has been mostly derived not from the laboratory, nor even from the dead-house, but from a study of the disease as we see it clinically in the camp, field hospital, in the ward, and by the bedside of the private patient. Perhaps it is meet for me to at first confess that this experience has taught me more humility than pride, and more caution and respect than positive opinion and definite conclusion. Nonetheless I feel quite confident that the victories of the physician are never more certainly won elsewhere in the practice of medicine than is often the case with pneumonia.

As you know from the teachings of your pathologist and of your bacteriologist, there are several, even many kinds of acute pneumonia, but in so far as the therapist is concerned much of this detailed knowledge is unnecessary, even inadvisable, if it be secured at the sacrifice of the patient's rest, through a delay in treatment, or if your basis of treatment be determined by theoretic conjectures and busy-body and exhausting physical examination.

Remember at all times that the chief point in the management of acute pneumonia is that you are treating a patient with an inflammatory condition of his lungs rather than some specific, definite, and unmixt infectious process. Please do not misunderstand me to suggest that you neglect proper physical examination, the use of the fluoroscope and x-ray, the thorough study of the sputum, the blood chemistry at times, the study of the expired air and of all phases of disturbed lung

physiology, careful study of the urine, and all this, but my point is that in such studies one must at all times consider first the condition of the patient, his well being and comfort, rather than the details of his disease process. The gross clinical aspects of the case are almost always of more consequence than any of the more detailed data secured by the finer methods of study. In this disease especially we must treat the patient, not nearly so much the disease.

Of course you must know, and it requires no very exhausting examinations to determine, if you are dealing with a senile pneumonia, one developing in the course of a surgical case or in an influenzal epidemic, nor must one forget the customary environment of the patient, those cases in the tropics or in citizens of the tropics often demand quite different procedures, for example, than cases developing among our own citizens here in this temperate zone.

Your patient must be put to bed, we shall all entirely agree on this point, but if the case occur in old age or in the course of surgical disease I am also quite certain that we shall not insist on the absolute dorsal position in bed. Rather we shall raise him gently up on the bed-rest, shift him from side to side, even bolster him almost upright in bed if thereby we relieve his cyanosis, discomfort, and dyspnea instead of, as in the average adult or juvenile type, encourage his lying flat in bed. If this position cause more pain than the patient finds appears by fixation of the involved side by lying on it, it stands to reason that we shall permit or encourage this rather than fight the pain and irritation by morphin and codein. In influenzal cases also I believe that we, as a rule, get better results by not lowering the temperature of our sick room, but rather by elevating it. Warm air may be none the less pure and oxygen rich than cold if we but exert our ingenuity in the control of ventilation and heat. Physicians practising in the tropics tell us that their patients do far better in warm atmospheres than in cold, and in my not inconsiderable experience with patients from these countries falling ill here I, too, have found, as a rule, that warmth is better than the cold which you and I and most of our patients

prefer. Never forget to seriously consider the comfort of the patient in the treatment of this disease

As to the outdoor treatment of pneumonia, I am personally very partial to it, but it depends much on weather conditions, customs of the patient, and somewhat on the extent and type of the infection. That preferable, however, is usually a matter easily determined. Move the patient's bed out on the veranda, or open all the windows, and if his cyanosis or dyspnea are relieved, this is the right thing, he will probably rest better, eat better, excrete better, and get well faster and in more comfort. If, on the other hand, he becomes more dyspneic, if his hands and feet and the tip of his nose become cold, if he becomes more restless or delirious, move him back into his room, see that abundant air is present, but have the room well warmed. Be very cautious how you expose the outdoor patient in examinations, in the use of the bath, the urinal, and bed-pan. Chilling of the skin surfaces is quite as capable of doing harm as good. Very few of us are alarmed now by the high temperatures of pneumonia, and very few of us use other agencies for the reduction of temperature than sufficient ventilation. My personal results in the use of hydrotherapeutic measures other than cleansing the body by gentle and not too tiring sponge-baths, tepid rather than cold, has not been satisfactory, and I have studied under and observed closely the methods of Dr. Baruch, who we all admire and reverence because of his intimate and skilful adaptation of hydrotherapy. I had the benefit of his assistance, instruction, and cooperation in my pneumonia wards at Camp Upton in 1917, but it has but crystallized my former ideas on this subject.

May I digress right here and say that I believe that the sputum should be secured and typed just as early as it can be obtained, even before the diagnosis is absolute, for I know that while the use of Type 1 serum in Type 1 pneumococcus infections is a splendid thing, it is not 100 per cent perfect any more than any other therapeutic measure. I speak of this here for the reason that I must insist that if you contemplate the use of serum, you must first type the sputum, for I am

convinced that the serum, all sera, particularly the polyvalent ones, are harmful except in Type 1 cases. Further, and this is why I consider this method now and here, if the serum cannot be given early, within the first forty hours of the infection, I much prefer not to use it at all, even in Type 1 infections. I cannot go here into the reasons, but you will find that my conclusions are those to which most clinicians of wide experience have arrived.

When I was a student and an intern practically all physicians believed more or less firmly in the use of local applications in some form applied at least to the involved side. I believe that my professor of medicine, Dr. George B. Dock, did dissent, but the average physician insulated his patient in quilted pneumonia jackets, cupped him, blistered him, applied some form of ointment or cerate—*did something* to his chest, perhaps only strapped him with adhesive. Few of us do these things now. It may be quite true that, as argued then, at least they do no harm, but in most, except unconscious cases, these methods all cause discomfort, and this is important, they make him more restless in bed, harder to examine without undue manipulation, and, in my opinion, they do no good and often much harm.

I shall deeply resent it if any of my conferees ever commit such outrages on me when I cannot help myself, but there are still excellent physicians, mostly of the older generations, who do these things, and there are yet patients and more of their relatives who feel that they have not been properly treated without some of the inquisitional procedures. It is much safer after the Red Indian and Chinese method to thus treat a solicitous relative rather than the patient. Then at least you will do no harm and I think that you will do the patient quite as much good.

Venesection is a method, however, of very great value. There are few who will dispute its occasional utility in correctly selected cases. These are mostly those instances in which there is an overburdening of the heart, the extremities become much congested, cyanosed, the dyspnea is marked, the blood-

pressure is usually high, though it may fall at any time with a failing heart muscle. These patients are usually full-blooded adults, the overly plethoric and overly vigorous, though sometimes the measure seems also indicated where the lung involvement is very great. I rather suspect that in all such cases there is an overburdening of the right side circulation. Most of such instances are much improved at least symptomatically by a timely venesection. May we thus abort or terminate an attack of pneumonia? I cannot answer this question either for or against. I have seen some instances in which this seemed to be the case, but so also have I rarely seen cases of apparently advanced involvement suddenly terminate and defervesce without anything being done.

Just a few more words as to the specific treatment of pneumonia. I have already said what I wish to say in regard to the use of Type 1 serum in Type 1 cases. May I be permitted to say that I hope that eventually a serum or a vaccine may be discovered which will be equally as beneficial in other pneumococcus types, in the streptococcus cases, and so on. As many of you know very extensive clinical experiments along this line are now being conducted in Bellevue Hospital. I have great confidence in Russell Cecil, who is mostly responsible for this work, and I am correspondingly hopeful, but it has thus far not passed beyond experiment, and the mortality rate in pneumonia is such a variable thing under different environment and in different epidemics that we must be very cautious in our conclusions.

Foreign sera are being used. Joseph Miller and Joseph Capps, of Chicago, have something to say in favor of these experiments, and their opinions carry as they must considerable weight, but, naturally, such men are very cautious as yet in their claims. Vaccines are being used particularly in streptococcus and in influenzal cases. As these experiments are being conducted they are certainly doing no harm in the hands of the careful men who are mostly making these studies, but beware as yet of commercialized specific products.

Dr Solis Cohen, of Philadelphia, a most experienced and

careful clinician, a man of sober and scientific thought, has used for a long time a method chiefly characterized by the administration of large doses of quinin. No doubt he gets good results, no doubt there is something in his method beyond his own art and skill in its use, and of all the other general measures which he employs, but I rather surmise that the latter is the more important. The iodids have been advanced as of specific value. I am quite certain that in syphilitics particularly they are of great utility, especially in the stage of resolution. A well-known New York clinician employs the salicylate of soda in selected cases with apparently good results, and so on, sodium chlorid, ammonium salts, and various biologic products are being advanced as of specific value. You may employ them judiciously if you like, probably you will at least do little harm with them, but do not neglect to use also the well-established methods which we do know, through treatment of the patient, help in pneumonia. Let us never forget also that a great deal of harm is doubtless done to patients by meddling and over-treatment. Nature herself is oftentimes a better physician than art.

According to the pathologic anatomist, most fatal cases of pneumonia show myocardial changes of a serious nature, and most clinicians of wide experience admit that death in pneumonia is commonly of cardiac type. It is but fair and just to say, however, that these opinions are now widely questioned, particularly by laboratory workers and to some extent by physiologists and chemists on the basis of important data discovered along the lines of research, perhaps as yet not fully understood or correctly interpreted. At any rate, nearly all clinicians feel that in the management of a case of pneumonia the circulatory problem eventually becomes the dominant one. On this pathologic-anatomic and clinical basis is doubtless founded the now well-nigh universal use of cardiac stimulation in pneumonia. Venesection is doubtless the first outgrowth of this conclusion and secondarily is the employment of drugs of the digitalis group.

Very many, I think most, clinicians advise now the use of

digitalis or of some member of this group in the pneumonias, at least in those cases which show circulatory embarrassment. A considerable group of us, and I number myself as of this party, feel that cardiac failure is of so frequent occurrence in this disease that a digitalization prior to the appearance of symptoms demanding its exhibition is an advisable practice. Of this group there are those who believe in digitalization by the rapid method, that is, by the administration of maximum doses very early in the disease, arguing that thereby they lessen their mortality rates by preparation of the heart for its inevitable stress. Others of us use it in most cases. I myself use it practically universally, except in children, or where the tissue involvement is slight, but I introduce the treatment by medium-sized doses gradually increased or prolonged until evident signs of digitalis effect are reached, cutting it down or out then except where circulatory strain is evident, on which occasion it is continued or even increased. In cases which from the outset show signs of circulatory distress, or in which a defective heart is known to exist, I digitalize by the rapid method.

I am strong in my belief that we are thus able to materially reduce our mortality lists in pneumonia. In a review which I made of over 5000 protocols of cases dying in the American Expeditionary Forces from pneumonia I believe that I found abundant evidence justifying this use of digitalis in pneumonia and bearing us out in the assumption that harm is rarely or never caused as a result of the method. Perhaps I am too strong a partisan of this method to give you a fair idea of it, but the very close touch which I was able to bear to literally thousands of cases of pneumonia in the army during 1917-18-19 causes me to feel that I am doing you and many of your clients a real service in most heartily endorsing this step in the management of your pneumonia cases.

Just a very few words as to the forms of digitalis which I have best used. The tincture, a physiologically tested and well standardized product, is my favorite, but I have used pulverized leaves, the infusion, digitol, digitoline, digalene, and other intravenous and hypodermic forms also successfully. You

must use the tool with which you are most familiar and in which experience has given you most confidence I have had particularly good results with various digitalis preparations secured from various pharmaceutic and pharmacologic laboratories connected with several universities I feel that this is a form of missionary work particularly commendable in our university research laboratories which have in the past too much neglected the dominant problems of therapeutics The tide has now happily well set in the opposite direction

Time does not permit me to discuss other members of the same type of drug—strophanthus, convallaria, and the like I think I am naming them in the order of their usefulness Digitalis for many reasons stands far in the lead

There are a great many drugs of emergency use in pneumonia Few of us, I think, use them, as it were, in the preparatory treatment of pneumonia as we do the digitalis group Most of them may be employed to tremendous advantage when the occasions for their exhibition arise, and this is why at the very outset of this talk I said that you would require for the correct treatment of pneumonia a very broad grasp of all therapeutic measures and arms Among such drugs to be considered as adjuvants to digitalis are caffeine and camphor, but you must remember that caffeine is likely to intensify delirium if it be present. Camphor effects are very short lived, however, in my opinion, though it not infrequently seems to be the frail and narrow bridge which spans the waning tide in many cases I think that it acts far better in digitalized hearts than when it is used alone Adrenalin has a real place Remember its pharmacologic action and study its effects in the particular individual in question before you exhibit it too freely Atropin is of very great benefit, but it has certain unpleasant drawbacks in its secondary effects on other organs than the heart.

You will not get into trouble with any drug in pneumonia, I think, if you always bear well in mind the pharmacologic effect of the drug and the anatomic chemical and clinical problems with which you are dealing The physician is tempted perhaps to try to go too deep into drug action in the consideration

of this problem, but he cannot know too much of them if he will treat pneumonia well. Again, however, I wish to point out to you the even greater danger of overtreating your cases. My own repertoire of drugs which I employ in most cases is extremely small. Digitalis is used in the average case however.

We older men all remember when the sovereign remedy in pneumonia, as in other conditions, at the time was oxygen. Then the method died a natural and little lamented death. The manufacturers, in their attempts to reestablish its popularity, ceased to paint the cans blue, so associated had fatalities and the "blue can" become in the minds of both patient and physician. Well, the oxygen treatment has been born again. It is urged once more, now on a chemical basis, because of a very narrow and ill-defined theory of the respiratory chemistry in pneumonia. It will take more than theory to reestablish it again in the minds of the experienced physician who during his intern days saw its failures and its very rarely beneficial results. It is of benefit in my opinion in certain cases of severe cyanosis due for the greater part to very extensive lung involvement, though it is by no means generally acknowledged as of value even here. It is entirely without effect in cardiac failure in pneumonia, no matter how efficiently it may be administered. It causes marked desiccation of the mucous membranes of the upper respiratory tract, and in my opinion is of far less value than the open window and a fan in the hand of a persistent nurse.

Of course it has been found that acidosis plays an important part in the death-rate from pneumonia. Again a contribution from the chemical laboratory. There is little doubt that the alkalis, particularly sodium bicarbonate, are useful when defective renal excretion becomes apparent from any cause. There appears little clinical utility for the method, however, except in such instances. If administered in a laxative form, as, for example, the oxid of magnesium, the laxative effect is doubtless useful, there are, as a matter of fact, few disease conditions which are not benefited by clearing of the bowel, and where the method does not cause too much annoyance and dis-

comfort high colonic irrigations with normal salt or sodium bicarbonate is doubtless useful. It is far better, however, not to attempt it when it involves too much manipulation of the patient.

In any case the bowel must be well opened, preferably, in my opinion, by the saline laxatives or, as just stated, by the alkalies. I rarely use active cathartics, however, and especially in the early stages I feel that enemata are the most desirable means of accomplishing this result. Unless the kidney action is defective (of course you will find albumin, casts, and sometimes blood-cells in the urine, but this is not a nephritis, simply a renal congestion in the ordinary case) I believe that it is well to give fluids in abundance, water, fruit juices, sweetened if desirable with milk-sugar, so that they have some considerable caloric value. Where the circulation becomes defective it may be advisable to limit fluid intake, especially if edema develop.

As a rule the feeding problem in pneumonia is unimportant until the period of convalescence. Milk, the fermented milks, fruit juices, and raw or stewed fruits are quite sufficient as a rule, and I believe that it is a very great error to try to introduce too much nourishment in this ordinarily short-lived acute infection. It is quite another thing during convalescence, however.

Now as to alcohol. Most of us use it at least in some cases. I do not myself ordinarily employ it except on the basis of a food, but I do feel that in very many cases diluted whisky or brandy may be very advisedly given. Champagne is also of real value, not as a stimulant, for I do not consider alcohol as such except in a very limited way, but the clinician who "never uses alcohol" in pneumonia has treated some of his patients in a very neglectful manner. In old age, influenzal cases, and in long-continued, slowly resolving cases I find it often of peculiar utility. Most skilled physicians at least use it. We must exact something more than a mere dogmatic social theory before we cast aside a drug which has been employed by our most astute physicians for so many years in pneumonia. The physician must not let his judgments be warped by the

propaganda of zealots or theologians I have no opinion to express on the use of alcohol as a beverage, my "clinical experience" in this line is very limited, but on the utility of it as an agency for the treatment of the sick, you and I are morally responsible if we permit the myopic zealot to wrest from our hands any agency or weapon which is of so real benefit in many disease conditions

I am entirely out of patience with the tendency shown in some schools to teach students that the treatment and relief of mere symptoms in the course of any disease is foolish, unscientific, and beneath the dignity of the physician. This is a particularly fallacious doctrine as regards pneumonia. As a matter of fact, the greater part of our active treatment in pneumonia except by the use of the sera and vaccines is symptomatic and nothing more. The relief of the symptoms is often the deciding point between the life or the death of the patient. Of course you must not strive to relieve symptoms to the point of doing the patient harm, of lessening his resistance against the infection, or of favoring the progress of the disease process. The physician who gives overdoses of morphin or codein in pneumonia merely to give comfort is quite as unartful, inconsistent, and unscientific as he who entirely refuses these most useful drugs when their adequate exhibition will quiet an exhausting cough, a distressing and agonizing pleurisy pain, or bring sleep to a tired and perturbed brain. Of course you will not use the morphin to the point of depressing the respiratory center, increasing the cyanosis and real dyspnea, but if you do not use it for its therapeutic effect in very many of your cases of pneumonia you will permit much unnecessary suffering, and will favor the progress of the disease and the loss of your patient's life because of the exhaustion which pain, lack of sleep, or irritating cough bring so frequently to the pneumonic

Tympanites is a most serious symptomatic manifestation in many cases of pneumonia. It seems particularly frequent, distressing, and dangerous in cases complicated by a diaphragmatic pleurisy, in many severely toxic cases, where the meninges are involved and doubtless in many other instances and condi-

tions which we understand but very vaguely as yet. It is a serious thing at all times, a symptom, but a most dangerous sign also. Of course you will attempt to relieve it by enemata, by colonic irrigation, by the ice-bag, sometimes by turpentine stupes, and so on, but every now and again you will find a case which responds so beautifully to pituitrin that you are cheered into the hope that at last you have found the sovereign remedy for tympanites, and in the next case it does no good whatever and may even seem to do much harm. As a rule I use first the mechanical means for its relief, I have indicated the most effective above, and then try tentatively and cautiously the pituitrin.

Still another very serious and unfortunately frequent symptom which will worry you many times in your management of these always serious cases of pneumonia is delirium. It may be present in the period of onset, it may be seen in the acme of the disease, or it may appear, as it most frequently does, after the crisis. It may persist for a long time during convalescence. Its mechanism is probably very various. Sometimes it is due to an effusion of serum into the pia-arachnoid, sometimes it is caused by a true meningitis, more frequently than not it appears as a result of something of which we know nothing or very little, we are likely to ascribe it to a toxemia. If we assume by this vague term the degenerative changes in the ganglion cells which appear as a result of the metabolic and exogenous poisons secreted or formed in the course of the infection, perhaps we are not so far wrong, but theorize as we will, the grave fact is that this is a symptom of pneumonia which is most difficult to control, one of very grave significance at any phase of the disease, and a condition which we must try to mitigate or control if possible.

When it is of mild type a good sleep produced by the administration of morphin, codein, adalin, chloral hydrate, or even by the bromids may entirely clear it up, more often than not, however it becomes a chief problem in the course of the disease, one which will sorely tax your ingenuity in drug use, in persuasion, tact, and in all of the devious channels of thera-

pusis which the good physician must explore in his attempt to give the patient relief.

I have but begun to indicate to you the symptomatic conditions which arise in pneumonia and which demand the best that is in you in the way of therapeutic skill, and my hour is nearly done. May I close this talk by reiterating the importance of the study and management of symptoms and of the individual in this disease?

Do not overtreat your patient. Use just as few drugs and just as many other physical measures as are demanded only. Disturb your patient just as little as possible. Do not examine him too frequently or too thoroughly just to satisfy your own curiosity. Try to bend every bit of knowledge which you possess to the relief of symptoms, to the support of the circulation, the promotion of excretion, and of rest in your case. It is very true that as yet we have very little to offer in the way of real treatment of pneumonia as a specific disease, but we have a tremendous field of effort which we may cultivate for the patient's relief. Stay with your patient as much as possible. Shape every sign and symptom to his benefit—that is the sort of "nursing" that cures pneumonia. Your close study and the application of your general knowledge of disease and therapeutics applied to the crisis as it develops may win the fight. You will, I doubt not, save many cases which would have otherwise died by just this individual study which I have suggested to you. You may not "cure pneumonia," but you can many times give life where but for you and your knowledge and effort death would have taken place.

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THE RÔLE OF THE CAPILLARIES IN CIRCULATORY DISORDERS

FROM long habit we have become accustomed, in our study of patients with disordered circulation, to direct our attention almost exclusively to the heart and to gage the progress of the case largely by the manner in which the heart reacts to the treatment that is given. A moment's reflection, however, will recall to our minds that, although the continuous action of the cardiac pump is essential to life, it is so only because it is the agent by means of which the blood is distributed through the body. The blood is the vehicle that brings oxygen and nutritional elements to the tissues and carries away the waste metabolites to the excretory organs of the body. It is distributed by the heart, but it is in the capillaries that its vital function is achieved. In other words, the whole circulatory system is adapted to maintain a continuous flow of blood through the capillary fields of the body, and it is when this capillary flow is impaired that symptoms of disease become manifest. A few illustrations will elucidate this point.

A patient with a failing heart is dyspneic and cyanotic in large part because the sluggish movement of the blood in the pulmonary capillaries, together with other mechanical factors which influence the capillary flow in the lungs, interferes with the absorption of oxygen and discharge of carbon dioxide from the lungs. The heart, it is true, is the ultimate cause of this, but the proximate cause lies in the sluggish capillary flow. Similarly, in Stokes-Adams' disease unconsciousness occurs because of the cessation of the capillary flow in the brain. It thus becomes apparent that we should direct more of our attention to the blood flow in the capillaries and consider the heart as only one of the factors which maintains this flow.

Physiologists have taught us that the circulation depends upon the proper action and coordination of the heart and arteries and veins, the most important of these factors being the intermittent pumping action of the heart, and the elasticity of the arteries, which converts the intermittent systolic output of the heart into a continuous stream. Important, too, is the peripheral resistance, which maintains a more or less constant head of pressure, and which has been thought of as dependent largely upon the degree of contraction of the smaller arterioles. In more recent years two other factors of importance have been emphasized, one, and the least well understood, is the elasticity of the tissues, the other, and it is the factor to which I wish to pay particular attention in this clinic, is the capillaries themselves. If it were true, as we used to think, that the capillaries are merely passive agents, and that the blood flow within them is determined by the state of the arterioles that supply them and the venules that drain them, a further discussion would be unnecessary. We have learned, however, that the capillaries take an active part in the distribution of the blood to the tissues by means of their inherent power of contractility and dilatability.

A very striking example of the importance of this action of the capillaries is their behavior in the condition known as "shock." For an understanding of this mechanism we are indebted to Dale and his co-workers and to Cannon. In brief, they have demonstrated that in "shock" there is a paralysis of the capillaries, as a result of which they become dilated and the blood becomes stagnant within them. When very many of the capillaries are thus affected they form a great reservoir of stagnant blood that is withdrawn from the circulation, so that there is insufficient blood in the heart and arteries to properly maintain the circulation. The injection of histamin into the body produces similar results and by means of it the mechanism of the reaction may be more carefully studied. Small doses of histamin, when injected, produce a rise in blood-pressure due to a contraction of the smaller arterioles. When larger doses are given there is still a primary rise in blood-pressure, which is soon exhausted, however, by a tremendous

fall and a condition resembling "shock" This is due to the fact that although the arterioles remain contracted, the capillaries have become paralyzed and dilated, so that the blood gradually becomes stagnant within them and thus renders ineffectual the arteriolar contraction Hooker has demonstrated photographically this paralytic action of histamin upon the capillaries

I have used this illustration of "shock" in order to emphasize how powerfully disorders of the capillaries may influence the state of the circulation, even when the heart and arteries are normal It will be of greater interest, however to study the behavior of the capillaries in the less acute disorders of the circulation

The human capillaries can be studied directly under a microscope by means of a device first described by Lombard If a drop of glycerin or castor oil is applied to the skin, and if this area is then observed through a microscope, with a magnification of about 75 diameters, while a strong light is directed upon it, the capillary loops in the skin can readily be visualized and studied Over most of the skin they appear as very small, comma-shaped loops and the circulation within them escapes closer observation However, at the base of the finger-nail or toe-nail, where the papillæ of the skin are flattened out, they are seen as beautiful, long, horizontal, hairpin-shaped loops, in which, under careful study and observation, the flow of the blood can be observed We are thus enabled to study the morphology of the capillaries, the character of the blood flow, and by means of a special instrument designed by Danzer and Hooker we can estimate the blood-pressure within the capillaries This instrument in essence is a small transparent air-chamber connected with a mercury manometer, by means of which pressure can be exerted on the skin, while the capillaries are kept under observation through the microscope The reading is made at the point at which the capillary flow reappears after the pressure which at first has been raised to the point at which the capillary flow was blocked, is released

THE MORPHOLOGY OF THE CAPILLARIES

It is difficult to define the normal appearance of the capillaries at the base of the finger-nail. Figure 191 represents, perhaps, the usual picture in healthy individuals. Here are seen one or two rows of simple loops just proximal to the cuticle, and below them many rows of shorter, more comma-shaped vessels. The difference in the appearance of these capillaries is due to the fact that in the first row the papillæ of the skin are flattened out so that the vessels are viewed running horizontally, while in the lower layers, where the papillæ are present, one sees only the top of the vertical capillary tuft. It is this arrangement of the papillæ that makes the finger the ideal site for the study of the capillaries, for it is only in the long loops that the blood flow and the blood-pressure can be properly studied. Over the rest of the body the capillaries present the appearance observed in the lower layers of the finger. Some German observers, particularly Weiss, have given elaborate descriptions of the capillaries in disease, and have drawn rather far-reaching conclusions from their studies. I shall try to show that in the present state of our knowledge most of these deductions are unjustified.

Weiss and some of his co-workers have described the following capillary pictures in disease. In arteriosclerosis the capillaries are present in normal numbers, but they are longer and more tortuous than in healthy individuals. In nephritis, both acute and chronic, the number of capillary loops is increased, and the individual vessels are longer and wider than usual and are greatly looped. In diabetes there is a point of dilatation at the junction of the arterial and venous loops of the capillary. With venous stasis the venous end of the capillary is greatly dilated. In both adults and children with vasomotor instability the capillaries are long and tortuous. This obtains particularly in patients with acrocyanosis.

These observations would be of real value to the clinician if he could be assured that the morphologic variations of the capillaries were of constant significance. Personal studies have convinced me that such generalizations can be made only with

reservations First of all, it is very difficult to define the normal As has been stated, Fig 191 represents the picture seen most commonly, but many variations are encountered Figure 192 is drawn from a perfectly healthy individual You will note the marked difference between it and the first illustration The vessels seen passing through the field from right to left are the subpapillary venous plexuses Usually they are not well

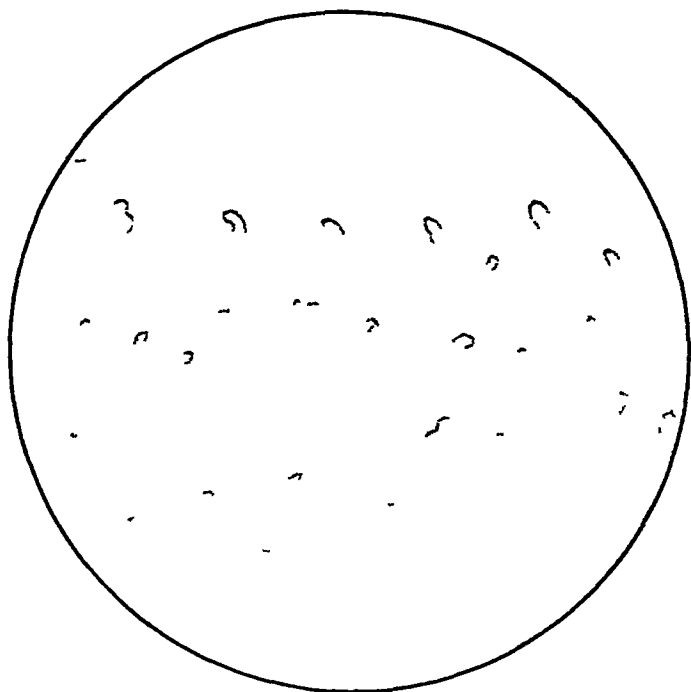


Fig 191 —Normal capillary picture

defined The other illustrations are taken from patients with varying pathologic conditions The name of the disease in each case is noted on the chart These few illustrations show that the matter is not so simple as it appears at first sight The classical pictures described by Weiss are not restricted to the diseases which he mentions, but may be found in a variety of disorders It is apparent, therefore, that in the present state

of our knowledge we cannot generalize and say that a certain capillary picture is pathognomonic of a certain disease. The most that we can say is that in diseases in which the vascular system is affected the capillaries tend to change in appearance, and that this change manifests itself chiefly in an increase in length and tortuosity of the vessels.

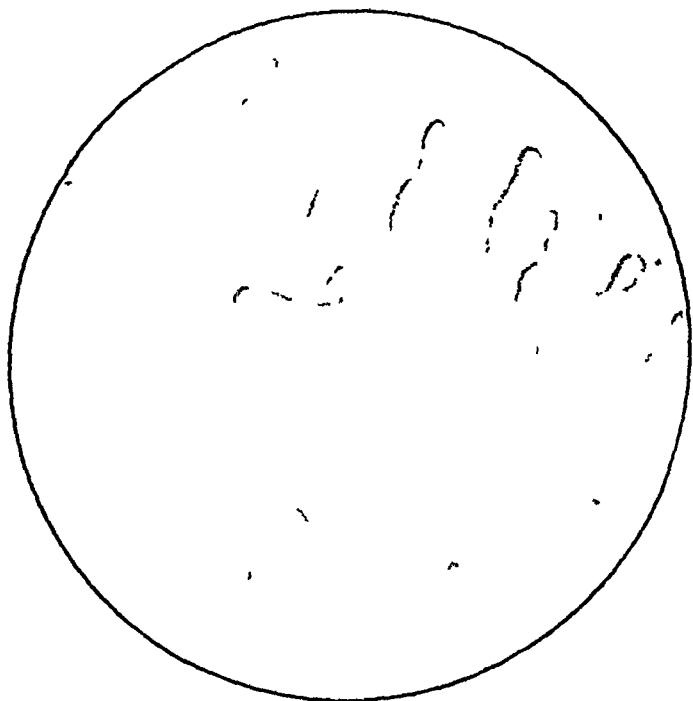


Fig. 192.—Normal individual. Long numerous irregular capillaries showing the venous loop in some entering the subpapillary venous plexus.

It will be of interest to recall at this point the similar change that the arteries undergo in disease. Disease of the arteries exhibits itself to the clinician either as a thickening of the vessel wall or as an increase in length and increase in tortuosity of the artery. The tortuosity is consequent on the lengthening of the vessel, for since the distance between the origin and termination of the artery remains the same, an increase in length

must manifest itself by a greater twisting and curving of the vessel. The same principle may be applied to the capillaries. Anything that tends to increase their length will tend to bring about a looping. Two chief factors come to mind as possible etiologic agents. One is an alteration in the capillary wall itself, and the other is a loss of tone due to abnormal nervous control. This point of view will enable us to understand why a similar appearance of the capillaries may be brought about by altogether different underlying causes. Thus both organic vascular disease, as well as imperfect nervous control, as found in patients with vasomotor instability, may bring about the same structural alterations in the capillaries.

The condition of the skin, too, apparently influences the capillary picture. One sees, not infrequently, an atrophy of the skin of the terminal phalanx. Under such circumstances the capillaries stand out very clearly in multiple rows of horizontal loops. This is due to the flattening out of the papillæ of the skin. Usually the subpapillary venous plexus is very prominent. It is possible, too, that the trophic disorder which is responsible for the thinning of the skin has acted on the capillaries as well.

In summary, we may say then that the morphology of the capillaries is not as yet of great value in the study of disease, but that further researches may demonstrate some facts of importance.

THE BLOOD FLOW IN THE CAPILLARIES

In the normal individual it is often difficult to visualize the flow of blood in the capillaries. There is uniform filling of all of the vessels in the microscopic field, and only after a close study will the streaming of the blood become apparent. The flow is rapid and constant and never pulsatile, and the blood column in the capillaries is a continuous one. Here and there a vessel may be seen in which the flow is sluggish at times, only to quicken in a few moments. Even in patients who exhibit a capillary pulse, such as is seen with particular frequency in aortic insufficiency, no pulsatile flow in the capil-

laries can be observed. I have discussed this point elsewhere and wish to emphasize here only that the term "capillary pulse" is a misnomer. The phenomenon is probably due to an increased pulsation of the small arterioles, and possibly of the venules.

The blood flow in the capillaries of the normal individual may be modified by various extraneous factors. Thus cold will retard the flow, while heat will accelerate it. This can readily be observed after cooling and warming the hand. When the capillary flow becomes slow the column of blood no longer has the normal continuous and uniform appearance, but is broken into segments separated by colorless areas. This may be called a "granular streaming." It is rarely observed in the normal circulation, and when present in many capillaries indicates some disorder of the capillary circulation. The flow of the blood in the capillaries may be artificially modified either by inflating a blood-pressure cuff that has been applied to the arm, or else by inflating the capsule of Danzer and Hooker's microcapillary tonometer. Under such conditions the capillary circulation may be altered at will, and the variations in the flow may be studied at leisure.

In certain disorders of the circulation a modification of the capillary flow may be observed. Probably one of the most frequent abnormalities observed is "granular streaming." This is seen not only when the flow in the capillaries is slowed but also when they have undergone a morphologic change. Thus it will be noted in patients with venous stasis due to myocardial insufficiency, as well as in those who exhibit the abnormal capillaries seen at times in arteriosclerosis and nephritis. Not infrequently complete stasis may be observed in several capillaries. The blood accumulates in the venous portion of the capillary, which becomes swollen, while the afferent arterial loop may empty itself almost completely. Then suddenly the venous loop empties itself and the blood flows again through the whole capillary with an increased velocity. These studies show us how abnormal the capillary flow may be in various circulatory disorders, but a further elucidation of the

fundamental significance of these observations still awaits further investigation

There is one condition, however, in which the study of the capillaries is particularly illuminating. I refer to the disorder known as acrocyanosis, the common affection in which the hands and feet become cold and blue or pale. Microscopic observation of the capillaries of these patients reveals, first, that the vessels often are abnormal in appearance. They are longer and more tortuous than usual and may present quite a bizarre architecture. With this it will be observed that during the period in which the hands are cold there is complete stasis in many of the vessels, and in the others the flow is sluggish and irregular. The blood-pressure in these capillaries is very low. Immersion of the hand in hot water provokes a remarkable change. The hand becomes bright red. Under the microscope we see the blood streaming rapidly through the capillaries, and that all signs of stasis have disappeared. At the same time the capillary blood-pressure has risen to a normal figure. We can thus attribute the symptoms of these patients directly to a capillary stasis induced probably by a spasm of the arterioles. The same conditions obtain apparently in Raynaud's disease, but in a greatly exaggerated form. Several German investigators have presented evidence to this effect.

The reverse picture is seen in essential hypertension. In these cases the blood flow in the capillaries is greatly accelerated, so that it becomes almost impossible to follow it in its course. All of these observations gain in significance when we come to the realization that most of these alterations in the peripheral blood flow, with the chief exception of the slowing due to venous stasis, are determined not by the heart, but by factors that lie intrinsically in the arterioles, capillaries, and venules. It is inevitable that such peripheral modifications in the blood flow, particularly when they involve wide-spread capillary areas, must react in turn upon the heart. It must be emphasized, however, that we are at present not in a position to draw far-reaching conclusions. The capillaries of the finger form after all only an infinitesimally small part of the whole capillary bed,

and of the parts unseen we can judge only by analogy. Moreover, the interplay of the many factors that sustain the circulation is so complex that the greatest circumspection must be observed in drawing generalizations

THE CAPILLARY BLOOD-PRESSURE

The capillary blood-pressure can be readily measured with Danzer and Hooker's microcapillary tonometer. It is important

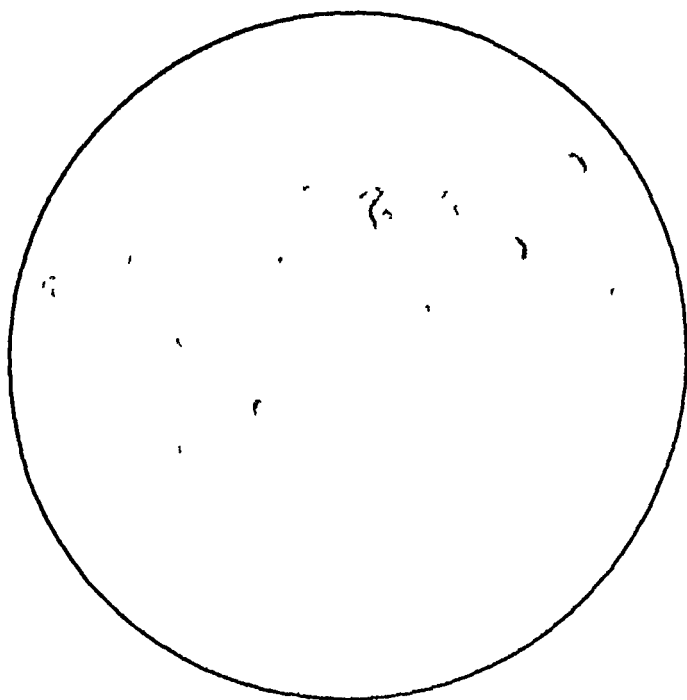


Fig 193 —Rheumatic mitral stenosis B P 184/100 Slight clubbing of fingers Capillaries numerous and rather tortuous Capillary pressure 4 to 10 mm Hg

to keep the hand at heart level during the estimation in order to avoid the hydrostatic effect of the column of blood The figures for normal individuals lie between 15 and 30 mm. of mercury Not all of the capillaries of one finger or of different

fingers will give the same readings. According to my observations the variability has been on the average 18 mm. There are many reasons for the wide range of figures. The blood flow in the individual capillaries is undergoing constant variations in rate and volume, dependent largely on the needs of the

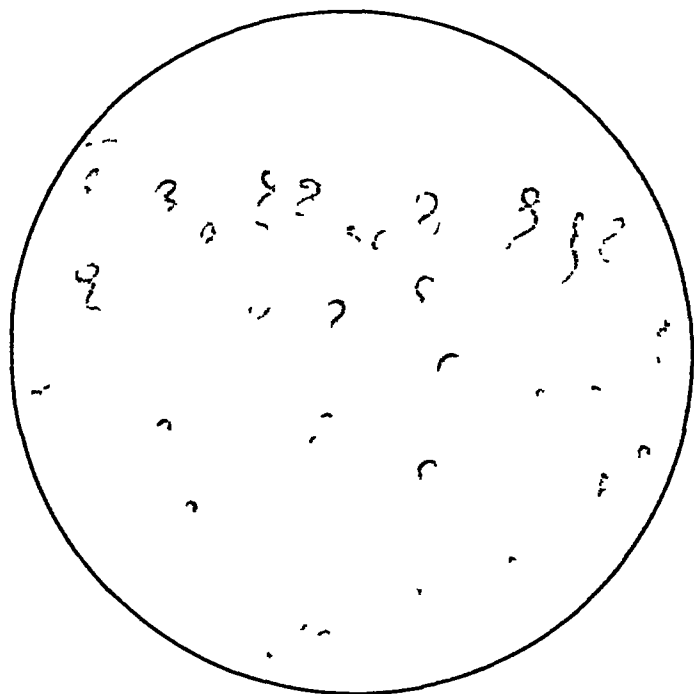


Fig 194 —Hypertension, arteriosclerosis, arteriosclerotic kidneys B P 180/100, slight clubbing of fingers. Capillaries numerous, long, many greatly convoluted. Subpapillary venules visible. "Granular streaming." Capillary pressure 20 to 73 mm Hg.

tissues. With this the pressure within them varies. In any particular capillary the readings are fairly constant at one sitting. Unless one makes a very large number of observations it is incorrect to average the readings, but a study of their general distribution in any particular case will tell whether the capillary pressure is normal, high, or low. When most of the readings

are above 30 mm Hg, one may be sure that the capillary pressure is high, when they are below 15 mm Hg, the pressure is low

I have had the opportunity of studying the capillary pressure in a series of patients with hypertension. The results are reported in detail elsewhere. We find that the cases fall in two

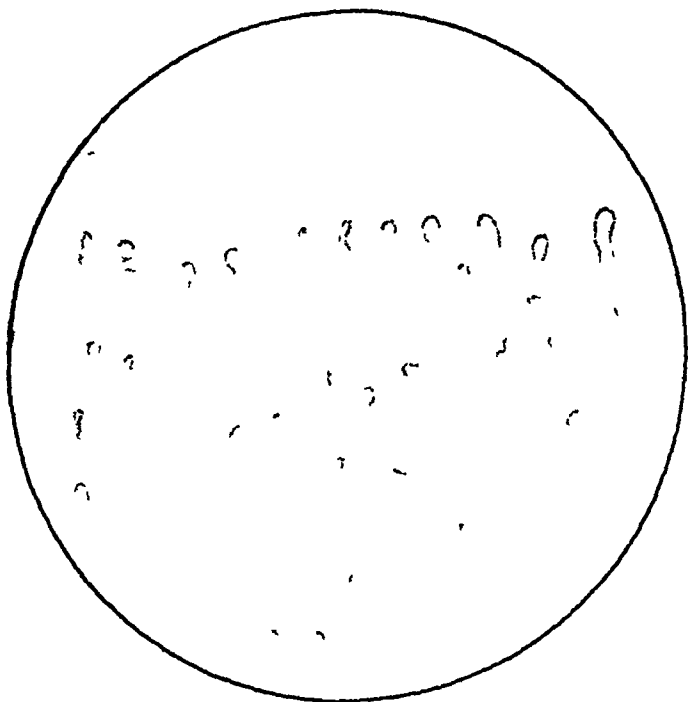


Fig 195—Mitral stenosis, auricular fibrillation, compensated B P 105 systolic. Capillaries numerous, rather thick. Many layers of horizontally placed loops. Subpapillary venules visible. Capillary pressure 17 to 29 mm Hg.

groups—those with high capillary pressure and those with a low or normal capillary pressure. In the first group the readings ranged between 30 and 75 mm Hg.

It is impossible to classify the patients clinically. Neither the history, the physical examination, nor a study of kidney function reveals any differential features. Similar urinary

findings are common to both groups, in both we find low as well as normal phenolsulphonephthalein excretion. There is no difference in the pulse-pressures in the two series. While it is true that on the average patients with a high capillary pressure exhibit a high diastolic blood-pressure, there are suffi-

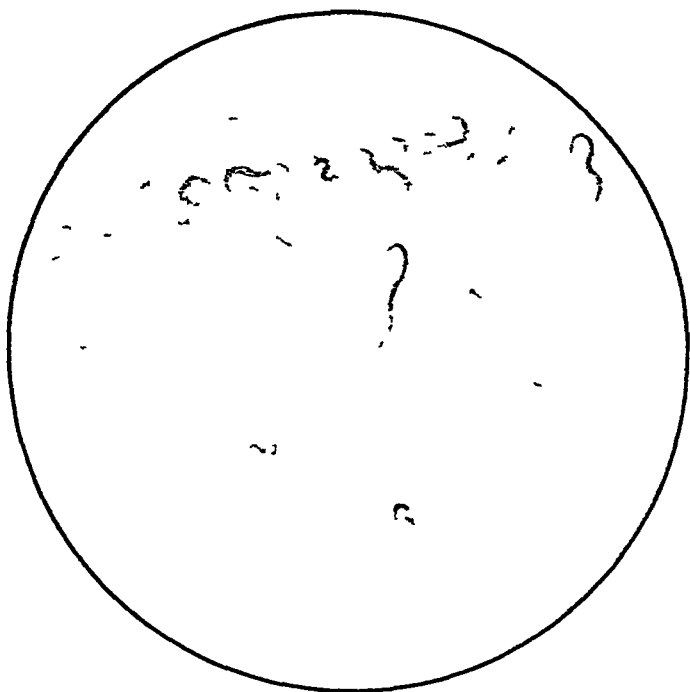


Fig 196—Mitral stenosis auricular fibrillation B P 105/60 Bizarre capillary picture. Great dilatation of venules and venous loops of capillaries. Capillary pressure 15 to 21 mm Hg

cient exceptions to this rule to invalidate any supposition of a causal relationship between the two

The problem of hypertension and its relationship to kidney disease still remains unsolved in spite of the innumerable searching studies that have been made. Opinion has veered from the extreme view that hypertension is always a result of kidney disease to the opposite extreme that all kidney disease is second-

ary to hypertension Both schools still have their advocates From the maze of facts and theories that have surrounded the subject, one thesis may be granted as established—that the syndrome of hyperpiesia or essential hypertension may exist without any evidence of nephritis Whether “nephritic hypertension” is a late stage of this or quite a different syndrome is

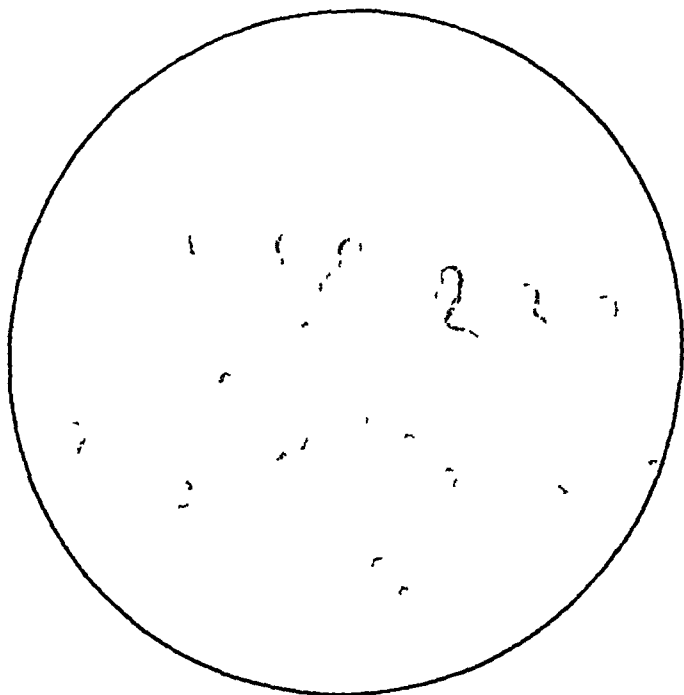


Fig 197—Pulmonary tuberculosis, slight acrocyanosis Venous loop of capillaries dilated Arrangement irregular Capillary pressure 15 to 20 mm Hg

unknown Blood-pressure studies have been singularly unilluminating in clearing up the matter We have learned to appreciate that brachial blood-pressure readings are very variable, and that in many instances they depend on the degree of contraction of the arterioles That the capillaries themselves may be concerned in the maintenance of this pressure was first brought

out forcibly by Dale and Cannon, who showed that a paralytic dilatation of the capillaries may cause a great fall in blood-pressure even when the arterioles are contracted. The reverse side of the picture, namely, that the capillaries may be a factor in the maintenance of high arterial pressures, is suggested by some of the studies of Kylin and of Weiss.

Kylin, using an instrument something like Danzer and Hooker's, has made some very interesting observations on the capillary blood-pressure in hypertension and nephritis. In glomerular nephritis he found the capillary pressure abnormally high in 100 cases investigated, but in benign nephrosclerosis with hypertension it was always normal. He studied 20 scarlet fever convalescents daily and found in some a marked increase in capillary pressure. In 3 of these patients a typical glomerular nephritis developed with albumin casts and red cells in the urine a few days after the capillary pressure had risen. He summarizes the results of his studies as follows: There are two types of hypertension—the nephrosclerotic hypertension is an arterial, the glomerulonephritic, a capillary, hypertension. In the first form the brachial blood-pressure is much more labile than in the latter. The hypertension is not the result of the kidney disease, but the glomerulonephritis is a manifestation of a diffuse capillary injury caused by the toxins of certain acute infectious diseases. If Kylin's division of hypertensive states is a correct one, it may well be that those of our patients who showed kidney involvement with a low capillary pressure did not fall within the group exhibiting glomerulonephritis and general capillary disease. As a matter of fact, autopsies of 2 of our cases support this belief.

When we recall that experienced clinicians have recognized the impossibility of diagnosing the anatomic lesion in the kidney from the clinical picture, particularly in chronic nephritis, we are in a position to understand why, in the cases that we have studied, we have been unable to predict which cases will exhibit a high capillary pressure as one of the manifestations of a glomerulonephritis. If our postulates hold true, however, and for confirmation we must await postmortem examinations

on appropriate cases, the estimation of the capillary pressure may prove an important aid in the differential diagnosis of glomerulonephritis from other types of kidney disease. It is not, however, of value in the differentiation of nephritic from essential hypertension.

As a rule, in essential hypertension the capillary blood-pressure is low. This may be attributed to a contraction of the arterioles. Any constriction of a vessel raises the pressure central to the obstruction and lowers the pressure peripheral thereto. Thus the view that in essential hypertension there is a constriction of the arterioles is confirmed. Low pressures are found as well in a number of other conditions. In the capillaries of fingers that are clubbed, or in which there is a vasomotor disturbance, as in acrocyanosis, the pressure is low. It is probable, however, that under these circumstances the low pressure is not universal throughout the body, but exists only in the extremities.

It will be seen from this general survey that the capillaries play an important rôle in disorders of the circulation. The study of the significance of capillary disease has just begun, and offers to clinicians as well as to physiologists a fruitful field for future research.

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CLINIC OF DR A S BLUMGARTEN

LENOX HILL HOSPITAL

THE ENDOCRINE FACTORS IN SOME COMMON FUNCTIONAL DISEASES¹

- (a) The Diagnosis and Treatment of Pituitary Headaches.
- (b) Adrenal Cortex Therapy in Hyperthyroidism and Functional Thyroid Disturbances

THE attention of the medical profession has until comparatively recently been devoted largely to the recognition of pathologic changes in organs. Very little attention has been paid to those patients who are unfortunate enough not to have any serious organic disease. A good deal of progress has been made, however, in the development of methods for the early recognition of anatomic changes in viscera, and we should not lessen our efforts to develop such methods. Any structural change that can be recognized at the present time, however, even by the most careful method, is gross at best.

Where there are structural changes in organs there are also changes in the functions of those organs. As a rule changes in structure and changes in function go together, but there is frequently quite a variation between the degree of structural change and the degree of functional change. There may be very little structural change in an organ and yet profound disturbance in physiology. Consequently, we divide diseases into those with demonstrable structural changes and those without such evident anatomic changes. The latter group of diseases are called functional for want of a better name. In actual practice the functional diseases constitute by far the largest group of conditions we have to deal with. It is quite

¹From the Endocrine Clinic

improbable, however, for change in function to occur without change in structure, but it is conceivable to have such structural changes develop and produce profound disturbances in function without being able to recognize the underlying pathologic changes by our present methods.

In order to deal, then, with the so-called functional diseases we must bend our efforts in two directions. First, to develop methods for the recognition of the characteristic structural change, and second, in the interim we must learn to recognize abnormal physiology, and attempt to develop methods of treatment to modify this abnormal function. As far as the patient is concerned, even in organic diseases, what is disturbing is not the pathologic change, but rather the disturbance in his normal physiology.

I shall present a number of cases this afternoon to demonstrate the rôle of the ductless glands in a few common functional diseases, to indicate the method of establishing the underlying endocrine basis, and to develop a form of therapy based upon such analysis.

The ductless glands play a tremendously important rôle in medicine and the importance of this rôle is constantly being more appreciated. It is unfortunate, however, that the entire subject of endocrinology has been somewhat discredited by the numerous and unwarranted therapeutic claims of highly advertised organic products. But behind the cloud of dust thrown up by these extravagant therapeutic claims many serious workers have made real live contributions to medical progress. What is needed, however, for the progress of this branch of medicine is thorough, painstaking, honest, unbiased study and accurate clinical observation.

Indeed, most of the progress in endocrinology has come largely through accurate clinical observation, and such observation is the most constant factor in medicine. At the present time laboratory methods seem to dominate medical practice, but one can make just as many errors with a test-tube as in clinical observation. Because of the difficulty of clinical

of the ductless glands our examinations

and analyses of the patients must be infinitely thorough, and we must use our judgment in separating the facts from the visions. The appreciation of the endocrines in medicine can only come from a thorough knowledge of the physiology of the ductless glands or at least as much of it as we understand at present. We can learn much, however, about normal physiology, as well as abnormal physiology, by a thorough study of patients.

Although endocrine study consists of several phases, such as the recognition of the frank endocrine syndromes and their *forme fruste*, the recognition of disturbances of the ductless glands in various infectious and other diseases, I shall devote my attention this afternoon only to the discussion of their rôle in the so-called functional diseases.

I do not mean to imply that the endocrine glands are the only factors concerned in functional diseases, but I shall attempt to demonstrate that they are the most important factors, and that at any rate they constitute the mechanism through which disturbance in function can take place. For example, a man may have business cares and worries which may upset his endocrine balance, resulting in adrenal insufficiency or hyperthyroidism, but there is only one way to relieve him of this condition, not by organotherapy, but by the readjustment of his business worries which underlie the condition.

The study of the ductless glands in functional diseases is perhaps the most important part of endocrinology. There is a good deal of evidence which indicates this important rôle. Speaking generally, we find that the ductless glands constitute the regulating mechanism of the physiology of the body. Let us briefly review, then, some of the essential facts that at least strongly suggest, even if they do not establish, this conception.

The thyroid gland controls metabolism probably by the elaboration of thyroxin. Physiologically speaking, it therefore controls the speed of function, such as the speed of cerebral activity, the speed of carbohydrate metabolism, the speed of practically all somatic functions, chemically it controls nitrogen metabolism. There is a good deal of evidence to show, and Rogers has demonstrated experimentally, that the thyroid

gland is a great sensitizer of the autonomic nervous system. It is generally agreed that the autonomic nervous system is an important factor in determining visceral function, and since the thyroid is the great autonomic stimulant the speed of visceral function is to a great extent dependent on thyroid activity. The thyroid also controls the iodine concentration of the blood, and probably has a good deal to do with immunity.

The pituitary gland controls the bony and skeletal growth and development. It plays an important rôle in controlling genital development. It is also an important factor, and possibly initiates various rhythmic functions, and it is, therefore, probably an important factor in such rhythmic functions as menstruation. Chemically, there is evidence to show that it is probably a controller of phosphorus metabolism, and therefore is important in the physiology and development of those organs where phosphorus metabolism is an essential, such as bony growth and cerebral development and physiology. It also has to do with the storing up of sugar and possibly with salt metabolism, and certainly with water metabolism. The rôle of the parathyroids in calcium metabolism is definitely established and they are important in maintaining the acid base equilibrium of the body.

The adrenal glands are necessary and useful organs in normal physiology. They control the somatic changes incident to emotions, they institute the physiologic changes necessary for combat and for emergency responses. Chemically, they probably liberate sugar from the liver for catabolism.

Looking at the various functions broadly, then, we find that essentially the ductless glands are controlling organs, the thyroid controlling speed of function, we might say that the pituitary controls volume, in growth and development, rhythmic and specific metabolic functions, and that the adrenal controls emotional response and emergency response, while the parathyroids probably control the chemistry for nervous activity and maintain tone of the nervous system. The genital organs give character and individuality to function. Apart from their distinctly sexual function they play an important rôle in

maintaining the secondary sex characteristics of the individual. In addition to the distinct definite sexual characteristics there are characteristics in function which are distinctly masculine or feminine, such as initiative, the domination of reasoning powers, or of emotions in the psyche, etc., are concerned. They are, therefore, important factors in psychic functions. Thus there is a distinct difference between the psychology of the male and that of the female, and this essential difference is manifested not only in the essential psychology, but probably in visceral physiology as well.

The rôle of the thymus, pineal, and other glands in physiology, while not having been definitely established, at any rate is such that they have controlling influences at various periods in life.

The functions of the autonomic and sympathetic nervous systems are tremendously important in maintaining physiologic function. Each organ of the body is supplied by branches from the autonomic and from the sympathetic nervous system. It is generally believed that except in the lungs the autonomic nerves carry the impulses for stimulating function, and the sympathetic, impulses for checking function.

There is a close relation between the ductless glands and the autonomic and sympathetic nervous systems, but whether the autonomic and sympathetic impulses are behind the ductless glands or whether the reverse is true is a moot question. There is a good deal of evidence to show that the secretion from the ductless glands sensitizes the autonomic and sympathetic nerve terminals. The thyroid is believed to be the great autonomic stimulant. Rogers has been able to demonstrate this experimentally on animals. The adrenal glands, as is well known, are the great sympathetic sensitizers. The relation of the other ductless glands to the autonomic and sympathetic nervous systems is not so well known. Where there is evidence of excessive autonomic function we must look to the thyroid or some other of the ductless glands for the cause, and where there is evidence of excessive sympathetic activity we must look to the adrenals.

I have merely discussed briefly the underlying basis for the understanding of the endocrine factors behind functional disease. In most functional diseases this can be demonstrated, but in others it is not so apparent because of the various factors playing a rôle in functional diseases. For example, in a gastric neurosis with hyperacidity there may be an underlying hyperthyroidism because of the evident excessive autonomic activity. In other diseases this cannot be demonstrated so readily.

There may also be a distinct anatomic basis for the endocrine disturbance in a functional condition, thus a disproportion between the size of the pituitary and the sella turcica which encloses it may give rise to characteristic symptoms.

In the study of functional diseases one must understand the normal physiology of each patient, but this is frequently a variable factor, for there are all sorts of normals. Keith and others have demonstrated that individual and racial characteristics in anatomy, in physiology, and even in psychology, as well as characteristic reactions to diseases, are dependent upon the domination of one or several ductless glands in the physiology of the individual. Thus we have as a normal various types, such as a thyroid dominant type of patient, a pituitary dominant type of patient, a gonadal dominant type of patient, with their combinations. Several combined types can be recognized, such as a pituitary-adrenal type, a thyroid-gonadal type, and a thyroid-adrenal type. While Keith's work has not been generally accepted, the appreciation of some of these individual variations in normal physiology is of tremendous importance in understanding many functional diseases. Practically, however, it is extremely difficult to recognize the combinations, although the simpler types are more easily recognized. In functional diseases each patient reacts in accordance with his individual physiology, and it is therefore essential to understand what each patient's particular normal is.

The value of appreciating the endocrine factors in functional diseases lies especially in the fact that they may give us a guide to therapy, not only to organotherapy, but to other rational means as well. The results obtained in classical forms of thyroid

deficiency by thyroid extract, even when given by mouth, strongly suggest that, given a definite similar deficiency of other ductless glands and an active organic product of the deficient, results can be obtained in other conditions. It is hoped, therefore, that because functional diseases are characterized by disturbance in physiologic control of function, we shall be able to treat these cases by organotherapy whenever there is a recognizable glandular deficiency behind the functional disturbance. The present problem in these conditions, however, consists in demonstrating a deficiency, and second, in obtaining a proper organic product. At the present time, in spite of the numerous claims made for organotherapeutic products, there are only a few substances which are distinctly valuable. Apart from adrenalin and pituitrin, the most reliable substances are thyroid extract as a specific for thyroid deficiency, and pituitary extract is useful for some symptoms of pituitary disturbance. I shall demonstrate a few cases this afternoon to indicate the method of endocrine analysis in a functional case. I shall also present a few cases of functional pituitary headaches and some cases of functional hyperthyroidism that have responded well to rational organotherapy based upon a demonstrable deficiency. Such method of treatment, however, is not always successful, and I shall show the failures as well as the successes.

PITUITARY HEADACHES

One of the most common functional conditions that is met with in practice is pituitary headache. One must not assume that all headaches are of the pituitary type. Before undertaking an endocrine study of a case all evidence of organic disease must be eliminated. Having eliminated such evidence and having as a chief complaint the headaches, it is essential to establish their character.

Pituitary headaches have certain definite characteristics. They are usually bitemporal or supra-orbital in character, and occasionally they are present on the top of the head. Frequently they begin in the occipital region, extend across the head

to the temporal region and to the frontal region, where they remain. They are usually periodic in character, although they may be present all the time. They may appear a day or two before or during menstruation. At any rate, whether they occur only at that time or continually, they are always worse at the menstrual period. These headaches are not infrequently accompanied by fainting spells, or attacks of dizziness, or blurring of vision, and occasionally by polydipsia and polyuria. The headaches are made worse by anything which involves pituitary activity, such as the ingestion of carbohydrates or menstruation. They usually disappear during pregnancy, especially from the fourth month on, but as soon as the child is born the headaches recur.

The examination of the patient always shows evidence of pituitary markings of one kind or another, anatomically, or singular pituitary physiology, and a pituitary psychology. The patients are usually of the Froelich type or acromegalic type, with changes in the secondary sexual characteristics, such as amenorrhea, sterility, etc. The female patients frequently have more or less of a feminine psychology and the males the reverse. In female patients these headaches are frequently associated with dysmenorrhea and in male patients with impotence.

The basis for treatment of pituitary headaches is the fact that physiologic hypertrophy of the pituitary gland in a small sella turcica gives rise to the characteristic headaches, consequently, the feeding of pituitary extract or the injection of pituitrin supplies a substance which removes the need for pituitary hypertrophy, thus relieving the headache. In most instances the results of such therapy are definite, although there are instances in which it is unsuccessful. On theoretic grounds, because the pituitary headaches disappear during pregnancy and because placenta and corpus luteum are the only new elements in the endocrine physiology at that time, they are also used for the relief of pituitary headaches, but in my experience these substances have not been very successful, although an occasional favorable result is obtained.

The burden of proof in all clinical endocrinology is always

on the endocrinologist, and since it is incumbent upon me to prove that the headaches I have just described are pituitary in nature I shall first present a case of a definite pituitary tumor showing the same type of headache on an organic basis

Case I Pituitary Tumor with Pituitary Headaches —A B
 A young, single girl of eighteen, by occupation a packer in a warehouse, came to the clinic January 4, 1922, complaining chiefly of amenorrhea. She was perfectly well until about last May, seven months ago. At that time she stopped menstruating. She had no other symptoms when, a week before Christmas, in addition to the amenorrhea, she fainted during the night. She awoke the following morning with a bad headache and fulness in the head, which she thought was due to an upset stomach. She took some bicarbonate of soda, which did not relieve her very much, and then she fell in another faint and struck the back of her head. There was no distinct convulsion and she recovered in ten minutes. The following week she had a similar fainting spell and attack in exactly the same manner. Since the original attack she has had continued headache, especially when she goes out in the street. This headache is accompanied by a throbbing sensation in the head. The attack usually starts in the occipital region and extends along the left side of the head to the supra-orbital region and left temporal region, where it persists. The headache is relieved by resting, it is made worse by eating large quantities of carbohydrate food. She has no headache at night and frequently grits her teeth during the night. The headache is probably worse at what would be the menstrual periods, although she does not menstruate. Since the onset of the illness she has been gaining and losing weight intermittently. During the fainting spell she perspires very freely, but not otherwise. She is easily excited ever since the onset of the trouble. The bowels move regularly, although she suffers from a good deal of abdominal distention. Everything she eats seems to turn to gas. She had no convulsions and she complains of no disturbance in vision. Since the first fainting spell she has become very dull and drowsy, as though she could sleep all day long. There is no disturbance in hear-

ing or in any of the other sensations. She has had two similar attacks since the onset of the trouble.

She had scarlet fever, typhoid fever, measles, and pneumonia as a child, but no other illness.

Her menstrual history began at seventeen. She was always irregular. She would be regular for three months, and since then she has had amenorrhea. When she did menstruate it lasted three days, and the last time it lasted five days. As a rule she bleeds profusely. She had no attacks, no nervousness, no cramps, in fact, she felt fine during the months she menstruated. She is unusually fond of sweets, bread, and potatoes. She drinks a great deal of water at times, and at those times she passes large quantities of urine. She prefers the society of girls to boys. She was very bright at school. Geography and spelling were her best subjects and she does not care for music.

Her father is about forty-eight years of age, living. He is rather short and thin. Her mother is forty-eight years of age, medium stature, though she was stouter formerly. She has two sisters and one brother. One sister is thirteen, the other is eleven years of age. She has a brother of ten. The sister is almost as tall as the patient, but rather thin, and the brother is of medium stature. There is no history of epilepsy, goiter, diabetes, or any other constitutional disease in the family.

Examination—Measurements: Weight, 130 pounds, height, 65 inches, span, 63 inches. Lower extremities, 33 inches, upper extremities, 32 inches, torso, 30 inches. Circumference of head, 23 inches, of neck, 13 inches, of chest, 33 inches, of waist, 28 inches, of buttocks, 37 inches. Pelvis, 11 x 7½ inches. Pulse, 105. Blood-pressure, 136/70.

The patient is a rather tall, thin, apprehensive, nervous girl. The skin is somewhat dry, scaly, moderately tense. There is no rash, no acne, no tache, no Sergeant's line. There are a few pigmented spots above the right breast and on both forearms and one in the left lumbar region. There is a congenital fistula over the sacrum probably leading to a dermoid cyst, surrounded by a streak of long hair extending downward and inward to the anal orifice.

Hair distribution shows long, coarse brown hair on the scalp, with medium anterior and temporal attachment, with moderate quantity of hair over both forearms, pubic hair scanty with a feminine border, and there is marked growth of hair over both legs

The head is rather broad, well developed. The forehead is prominent and has prominent supra-orbital ridges. The ears are small, round, cyanotic. Examination of the auditory canal shows a normal drum membrane. The eyebrows are bushy, pointed at the edge. The glabella is of medium width. The eyes are blue. The pupils are round, equal. They react to

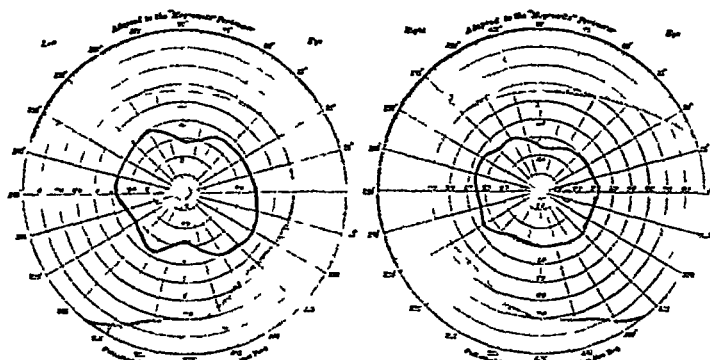


Fig 198—Case I A. B. Perimetric reading showing double contracted visual field in pituitary tumor

light and accommodation. There is a suggestion of exophthalmos and of internal strabismus. Graefe, Stellwag, Kocher, Dalrymple, and Mobius signs are all negative.

The face is broad, the chin is square. There is no prognathism. The teeth are in bad condition. There is a gold crown over the left upper lateral incisor. The upper front incisors are overlapping. The canines are sharp. The tonsils are flat, submerged. The throat is congested, the neck is long, the thyroid is not enlarged. The chest is rather wide, the breasts are of moderate size, the nipples are flat, and there is considerable pigmentation around them. The lungs and heart are normal. The abdomen is not distended. The waist is

rather narrow There are no areas of tenderness, rigidity, or masses felt

There is a lordosis and scoliosis of the lumbar spine The upper extremities are rather thin The hands are narrow The fingers are long, rather infantile, and there is a slight tremor The lower extremities are thin and show the hairiness above noted



Fig 199—Case I A B Roentgenograph of sella turcica, showing erosion of floor in case of pituitary tumor

Examination of the nervous system is negative except for slightly exaggerated knee-jerks The x-ray examination of the skull shows a large sella turcica with an erosion of the floor and very distinct posterior clinoids, suggesting pressure within the sella turcica

Eye examination by Dr Steinbugler Examination of the eyes shows vision 20/40, and a double optic neuritis more

marked on the right side than the left. In the right eye this amounts to a choked disk. The fields are concentrically contracted to about 35 degrees, no central color scotomata in either eye. The right eye is at a slightly lower level than the left. The findings point to intracranial pressure.

The urine examination is negative.

This patient was suffering with amenorrhea for about eight months. She did not feel sufficiently ill to consult a physician and only came to the clinic because of a fainting spell followed by stomach trouble to which she attributed her entire illness. The headache, however, was distinctly of the pituitary type, and thus directed my attention to investigating her constitutional make-up. We find evidence of intracranial pressure and erosion of the sella turcica associated with amenorrhea. The general make-up, the broad forehead and prominent supra-orbital regions, the hairiness, the overlapping teeth, the delay in the menstruation, all pointed to the pituitary. This was evidently her normal physiology. We assumed there was evidently some congenital disturbance in the pituitary which was probably the basis for the organic lesion with evidently a tumor, which was developing. The basal metabolism determination was not done, because it would have no bearing upon the condition. She does not show the usual bitemporal hemianopsia but she does show the evidence of intracranial pressure, a choked disk and contracted visual field.

I am presenting this patient merely to indicate the type of headache which occurs when there is a distinct lesion in the pituitary, in this case a tumor.

Case II Functional Pituitary Headache—R. B. A married woman of thirty-four came under observation in November, 1921, complaining chiefly of headache. She has had attacks ever since she began to menstruate. The headache is characteristically supra-orbital and bitemporal. If it is very severe it extends over the entire head. It is relieved by rest at night. Any excitement brings on a headache. It is periodic in character and she has it about three times a week. She has no blurring of vision but feels faint when it occurs. With some

of the headaches she has a severe pain in the eye with blurring of vision. The headache usually is worse either before or during her menstrual period. Occasionally it comes on after menstruation. It is frequently accompanied by a pain on the top of the head and by dizziness when she stoops over. It usually lasts about a day. She is inclined to be nervous, especially when she works hard, doing her own housework, and she becomes irritable, especially over little things. Her hands perspire moderately. She frequently has indigestion with her headaches. She feels drowsy at times in the afternoon. During pregnancy she is quite free from these headaches and feels better than at any other time. She has no attack at all during pregnancy and she feels very well at that time. She was much stouter as a girl, and about the age of eighteen or twenty years she began to be stout. She is very fond of music. In college she was very fond of mathematics and practical subjects. She is naturally of a calm, even disposition and practically inclined. She has a very even temperament, although she gets depressed occasionally. She frequently feels so nauseated that she vomits, at times her bowels move freely.

She had mumps, measles, scarlet fever, and chickenpox in childhood. She has had an attack of appendicitis and the appendix was removed. A year ago she had an attack of abdominal cramps which was called a stone in the bladder, but the diagnosis was not verified.

She began to menstruate at thirteen. She was very irregular in the beginning. It was always accompanied by severe cramp-like pains and lasted about seven days. She has been married about ten years. Since the birth of her child the menstruation has improved. She has no more pain and she is always regular. The labor was very prolonged. She has no other children.

She drinks a cup of coffee a day, is very fond of bread, which she likes more than anything else, she is not especially fond of meat.

Her father died about sixteen years ago. He suffered with headache, similar to the ones the patient has, but much worse. She takes after her father in everything, and similar headache.

have been common in her father's family Her mother is still living She is a tall, thin woman Her mother had goiter in her younger years There is no history of any other constitutional disease in the family

Examination —Weight, 135 pounds, height, $64\frac{1}{2}$ inches, span, $63\frac{1}{2}$ inches Lower extremities, $31\frac{1}{2}$ inches, torso, 33 inches Circumference of head, $21\frac{1}{2}$ inches, of chest, $34\frac{1}{2}$ inches, of waist, $28\frac{1}{2}$ inches, of buttocks, $37\frac{1}{2}$ inches Pelvis, $10\frac{1}{2} \times 8$ inches Pulse, 116 Blood-pressure, 130/70

The patient is a young woman of medium height, of rather broad stature, with a suggestion of puffiness over the skin The skin is smooth, soft, rather pale, there is a slight tache, there is no Sergent's line There is a marked absence of pigmentation

Hair distribution The scalp is covered by chestnut colored curly hair, with rather marked anterior attachment There is very slight hairiness over the arms and legs, and the border of the pubic hair is convex

The forehead is straight, broad, with rather prominent supra-orbital ridges, the face is broad, with square jaw, rather sad expression The eyes are rather dull, there is slight edema of the lower lid There is a suggestion of anophthalmos, which is probably due to the deep-set eyes The palpebral fissures are of medium width, with a suggestion of a Mongolian slant The eyebrows are thin, especially in the outer half The eyes are brown, the pupils are round, equal, react to light and accommodation, there is no nystagmus Graefe, Stellwag, Kocher, Dalrymple, and Mobius signs are all negative She wears glasses for astigmatism and far-sightedness The glabella is narrow, the nose is straight, of medium width, with a soft tip, the ears are rather long, very small, with rudimentary lobules The teeth There is no evidence of decay or purulent secretion Upper front incisors are broad and square On the right side there are a number of artificial teeth Both canines are artificial The lower teeth are pigmented but long and narrow The upper lateral incisors are very small The mucous membranes are very pale, the tonsils are small

The neck is narrow, somewhat long, the thyroid is palpable, but not enlarged. There is a fulness of the supraclavicular regions, especially posteriorly, which is suggestive of adiposity, but there is no cervical rib. The chest is well developed. The costal angle is acute. The breasts are large and pendulous, with an extensive light areola around the prominent nipples. There is no increase in the mediastinal area of dulness. The lungs and heart are normal.

The abdomen is distended due to a slight tympanites. No areas of tenderness or rigidity present. The liver and spleen are not enlarged. The lower border of the stomach can be made out a fingerbreadth above the level of the navel. The kidneys are not palpable.

Extremities The upper extremities are rather thin. The hands are narrow. The fingers are long and square. The hands are cold and moist, there is no tremor. The lower extremities are rather thin. There is no edema, no hairiness, there is moisture of the skin.

The examination of the urine is normal. The roentgenogram of the sella turcica shows no change in its size or structure. The basal metabolism is +8 per cent. The perimetric reading shows normal visual fields.

This patient is essentially a pituitary dominant type of patient because of the characteristic measurements, the span being less than the height, and the torso greater than the lower extremities, the rather broad features, the primary adiposity, the prominent supra-orbital ridges, the scant menstruation, the history of dysmenorrhea. Psychically she is unemotional, with a practical, matter-of-fact temperament. There was no evidence of any organic disease, the only findings were the constitutional make-up above described, which apparently indicates domination of the pituitary gland in her physiology. She suffers, however, from headaches similar to those of the previous patient who had a pituitary tumor. These headaches are characterized by periodicity, by a characteristic pituitary location, by being worse during the menstrual period, by improving during pregnancy. Since her marriage, however, a

new element has entered, such as the loss in weight the periods of excitement, the nervousness and slight tachycardia, which we might interpret as evidence of hyperthyroidism, to compensate for the subnormal gonadal activity due to her pituitary manifestations. Practically, however the patient came for the relief of her headaches which were very severe and had not responded to the usual methods of treatment.

She was placed on pituitary extract, 0.15 gm three times a day. About a week after beginning treatment she telephoned to state that her headaches had been relieved for the first time and that she had been without headaches since taking the medicine. A week later she went through her menstrual period lasting only five days with a scantier flow than usual, but accompanied by considerable cramps. She was placed on benzyl benzoate in doses of 1.5 gm for the relief of these pains. She returned three weeks after her first visit and stated that so long as she took the medicine she was free from headaches. At this time she was placed on pituitary extract, 0.3 gm, and at the present time she is free from the headaches. This patient illustrates a characteristic pituitary headache which has responded to pituitary feeding but she had dysmenorrhea during her menstrual period which was not relieved.

Case III Functional Pituitary Headache—R. S. A young girl twenty years of age came under observation in August 1921 complaining chiefly of headaches which were usually confined to the right temporal region and at times to the left temporal region and to the top of the head. They were always accompanied by painful menstruation. She was perfectly well until three or four years ago when she began to have headaches. These headaches would occur in the right temporal region, always on the top of the head and at times in the left temporal region. They were periodic and would occur once or twice a month and especially at the time of menstruation. As a rule they would occur just before menstruation but at other times they occurred during menstruation. The menstruation was usually accompanied by severe lower abdominal cramps. Because of the intensity of the headaches and the

The neck is narrow, somewhat long, the thyroid is palpable, but not enlarged. There is a fulness of the supraclavicular regions, especially posteriorly, which is suggestive of adiposity, but there is no cervical rib. The chest is well developed. The costal angle is acute. The breasts are large and pendulous, with an extensive light areola around the prominent nipples. There is no increase in the mediastinal area of dulness. The lungs and heart are normal.

The abdomen is distended, due to a slight tympanites. No areas of tenderness or rigidity present. The liver and spleen are not enlarged. The lower border of the stomach can be made out a fingerbreadth above the level of the navel. The kidneys are not palpable.

Extremities. The upper extremities are rather thin. The hands are narrow. The fingers are long and square. The hands are cold and moist, there is no tremor. The lower extremities are rather thin. There is no edema, no hairiness, there is moisture of the skin.

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She was placed on pituitary extract, 0.15 gm three times a day. About a week after beginning treatment she telephoned to state that her headaches had been relieved for the first time and that she had been without headaches since taking the medicine. A week later she went through her menstrual period lasting only five days with a scantier flow than usual but accompanied by considerable cramps. She was placed on benzyl benzoate in doses of 1.5 gm for the relief of these pains. She returned three weeks after her first visit and stated that so long as she took the medicine she was free from headaches. At this time she was placed on pituitary extract 0.3 gm, and at the present time she is free from the headaches. This patient illustrates a characteristic pituitary headache which has responded to pituitary feeding, but she had dysmenorrhea during her menstrual period which was not relieved.

Case III Functional Pituitary Headache—R. S. A young girl twenty years of age came under observation in August 1921 complaining chiefly of headaches which were usually confined to the right temporal region and at times to the left temporal region and to the top of the head. They were always accompanied by painful menstruation. She was perfectly well until three or four years ago when she began to have headaches. These headaches would occur in the right temporal region always on the top of the head and at times in the left temporal region. They were periodic and would occur once or twice a month and especially at the time of menstruation. As a rule they would occur just before menstruation but at other times they occurred during menstruation. The menstruation was usually accompanied by severe lower abdominal cramps. Because of the intensity of the headaches and the

severity of the abdominal cramps she always had to be confined to bed throughout her whole menstrual period. During the time when the headaches are severe she is quite drowsy and feels weak.

She is a nervous type of girl, she does not gain in weight, but at times perspires very profusely. About three years ago before the onset of this illness, she had stomach trouble, characterized principally by abdominal distention, but without definite gastric symptoms. Her bowels were very constipated. She has no falling out of the hair. Her hands perspire easily, but no other parts of her body.

She had pneumonia and measles as a baby. Otherwise the past history was negative. She began to menstruate at thirteen or fourteen years of age and was always regular. Her menstruation is very profuse and lasts eight days. It was always accompanied by the intense headaches above described and severe cramp-like pains. She always has to stay in bed throughout her whole period.

She is very fond of sweets, vegetables, and fruit, she drinks a cup of coffee in the morning and a cup of tea at lunch time. Her father died of appendicitis before she was born and is said to have been tall. Her mother is tall, not unusually stout. She has one brother, thirty-one years of age, who is tall and stout, one sister of twenty-three, taller than the patient, not so stout. There is no history of goiter, diabetes, or other constitutional disease in the family.

Examination—Weight, 82½ pounds, height, 61 inches, span, 60 inches. Lower extremities, 30 inches, torso, 31 inches; pelvis, 9½ x 6½ inches. Blood-pressure, 115/75. Pulse, 72.

The patient is a rather thin, dark complexioned girl. The skin shows no rash, but there is a long streak of light pigment over the lumbar vertebræ. There are two large pigmented spots over the left lumbar region. There is an area of pigmentation over the right knee. There is a pigmented mole over the right lower scapular region. There is a slight evanescent momentary tache. There is no Sergent's line. The skin is oily, smooth, and rather tense.

Hair distribution The hair over the scalp is thick, abundant, fine and silky, with a marked anterior attachment. There is downy hair over the arms and forearms. Profuse hair over the lower extremities. The pubic hair is of feminine distribution and the axillary hair is present.

The forehead is straight and broad. The supra-orbital regions are marked. The eyebrows are long and rather thick. The eyes are brown, bright expression, the palpebral orifice is of medium width. No exophthalmos, no nystagmus. Graefe, Stellwag, Mobius, Dalrymple, and Kocher signs are all negative. The pupils are round, equal, and react to light and accommodation. The ears are small, the lobes are free and unattached, the face is oval, rather broad. The jaw is square, but tapering. The nose is straight, the glabella is broad and the tip is soft. The teeth are in excellent condition, white in color. The upper front incisors are long and square, with slight ridging at the edges. There is increased interdental spaces. The lateral incisors and canines are prominent. The throat is congested, the tonsils are small. The neck is rather long, the thyroid is not enlarged. There are no supraclavicular fat deposits.

The chest is well developed, there is slight sloping of the shoulders, the costal angle is acute. The breasts are prominent. There is considerable pigmentation around the nipples, which are flat. The lungs and heart are normal. The abdomen is not distended. There is no tenderness or rigidity present. There is a markedly dilated stomach, the lower border being felt about a handbreadth below the level of the navel. The right kidney is palpable, the liver and spleen are not enlarged.

The general configuration of the body is of the feminine type. The extremities are thin, the hands are narrow. The fingers are long and square, the hands are rather cold and rather purple in color. The lower extremities show the hairiness above noted. There is no edema.

The urine examination is negative. The basal metabolism shows +15 per cent. The x-ray of the sella turcica shows a small contracted sella and an irregularity in the anterior clinoids.

which the x-ray man suggested was a fracture, but apparently it was not a fracture

This patient was suffering from characteristic pituitary headaches. They were periodic in character, they were bitemporal, and were especially severe during menstruation and accompanied by dysmenorrhea. Furthermore, the examination of the patient indicated the pituitary domination in her make-up. This was characterized by the coarse features, by the prominent supra-orbital ridges, the rather broad nose, the wide interdental spacing, the undersize and the characteristic pituitary measurements, the span being less than the height and the length of the torso greater than the length of the lower extremities. The sella turcica was small. There was no adiposity, however, and there were no secondary sex manifestations. The marked pigmentation and the loss in weight, as well as the asthenia, suggest thyroid overactivity, which is probably associative or compensatory.

The patient was put upon pituitary extract, 0.2 gm. three times a day. She returned a week later stating that for the first time her headaches were relieved. Two weeks later she came back stating that she had been through her menstrual period without any headaches and with diminished abdominal cramps during menstruation. She stated she was entirely different and was able to work for the first time during her menstrual period. She was given atropin sulphate, 0.0001 gm., in addition to the pituitary extract for the relief of her dysmenorrhea. This patient was on pituitary feeding for four months. She was free from headaches throughout this time, but she had slight dysmenorrhea at her menstrual period, which was usually relieved by atropin. At this time it was decided to try the effect of placental extract for the relief of the headaches on the theoretic consideration that pituitary headaches are relieved during pregnancy from the time the placenta is fully developed until the birth of the child. And since this is the most important new element in endocrine physiology during pregnancy, the relief of the headaches at this time might be due to a secretion from the placenta. She was put on placental

extract, 0.2 grains three times a day. She returned two weeks later stating that the headaches were slightly relieved, but the effect was not as marked as after the pituitary extract. During her menstruation she felt worse. She was kept on this treatment for four weeks longer, with the same results, and at that time she was again put back on pituitary extract in 0.3 gm. doses, and at the present writing she is free from the headaches, and she has gained $5\frac{1}{2}$ pounds in weight. Her menstrual periods are unassociated with pain; she is able to work, and does not have to be confined to bed any longer during her menstrual periods.

Case V Functional Pituitary Headache—M. de G. An Italian married woman of thirty-nine, came under observation in November, 1921, complaining of headaches.

She was very well until about four months ago, when she began to have severe headaches which were usually located in the right temporal region. They frequently begin in the occipital region and extend around to the temporal region, and are frequently accompanied by a thumping sensation in the head. The attacks are periodic. They usually last from three to four days, and then disappear for a period of from four days to three weeks. They are brought on especially when eating carbohydrate foods. She has no other symptoms. She does not perspire excessively; no gastric symptoms, her bowels are constipated. The past history was practically negative.

She began to menstruate at the age of fourteen, she was always irregular, her menstruation lasting from seven to eight days. During the menstrual period she has the severe temporal headaches above described and her menstruation is accompanied by severe dysmenorrhea. She has been married about nineteen years. She had 9 children, 7 of whom are living, she is now nursing a child and does not menstruate.

Her father died of pneumonia, her mother is alive, she is a rather thin woman, there is no history of goiter, diabetes, or other constitutional disease in the family.

Examination—Weight 116 pounds, height, 58 $\frac{1}{2}$ inches, span

57½ inches Lower extremities, 28½ inches, torso, 30 inches, pelvis, 10½ x 8 inches Blood-pressure, 115/70 Pulse, 82

The patient is a rather stout, fairly well-developed woman of dark complexion There is no rash on the skin, there is no tache, no Sergeant's line The skin is of olive color, rather soft, velvety, and oily There are no distinct areas of pigmentation

Hair distribution There is an abundant growth of jet black hair on the scalp, with an occasional streak of gray at the temples, with a marked anterior attachment There is considerable hair on the upper lip There is considerable hair over both forearms and legs, over the sacrum, and the pubic hair is feminine The axillary hair is present and the pubic hair has a pyramidal border

The eyes are prominent, the palpebral fissures are normal in width The eyes are dark in color, the pupils are round, equal, and react to light and accommodation Graefe, Stellwag, Mobius, Kocher, and Dalrymple signs are negative The nose is normal, rather broad, straight, with a convex tip The teeth are in poor condition They are crowded together, the upper incisors are rather broad, but twisted The neck is short, the thyroid is not enlarged

The chest is rather broad, the costal angle is wide The breasts are large, pendulous, with large pigmented prominent nipples that secrete milk The lungs and heart are normal

The abdomen is pendulous, with marked inguinal adiposity, and there is diastasis of the rectile muscles The stomach is dilated, the lower border extending about three fingerbreadths below the navel The liver and spleen are not enlarged, the kidneys are not palpable The urine examination is negative

The x-ray of the sella turcica showed a rather long, shallow sella with clubbing of the posterior clinoid and a very long, thin, narrow shelf extending anteriorly The basal metabolism was not done in this case

The patient is suffering with a characteristic pituitary headache She has the physical make-up which indicates a dominant pituitary physiology, namely, the coarse features, the hair over the upper and lower extremities, the adiposity,

the prominent supra-orbital ridges, and the characteristic pituitary measurements, the span measuring less than the height and the torso less than the lower extremities

She was put on pituitary extract, 0.15 gm, with a prompt relief of the headaches. She has been on this treatment until the present writing and has been entirely free from the headaches.

Case VI Functional Pituitary Headache in a Male —D L
A single man, a tailor of forty, came under observation in January, 1922, complaining of pains all over the body, with weakness and headache. The illness began about four years ago, when he had a fainting attack with unconsciousness lasting about ten minutes. He has not had a similar attack since but he has individual pains and sensations over the entire body. Ever since the onset of the illness he has been suffering with supra-orbital and bitemporal headache, which is periodic and associated with attacks of dizziness. The headaches are not influenced by diet. He has no excessive perspiration but has intermittent constipation. He has grown quite stout. When he is very nervous he is usually very constipated. He is very unhappy and morose, in fact, even melancholic. He prefers to be by himself and shuns company. He is sexually impotent.

He has never been ill before in his life. He denies venereal disease, but has been cystoscoped and treated with sounds for his sterility. He masturbated frequently up to the age of eight.

He is quite fond of bread and potatoes, drinks tea and coffee moderately, is inclined to be of a nervous disposition, worries very easily.

His father is dead, though he does not remember at what age, but his stature was very much like that of the patient. His mother is dead, but he does not remember much about her, the age and cause of her death are unknown. A paternal step-brother of the same stature as the patient died of gall-stones. He has one brother and one sister living, both resembling the patient in general stature. No other member of his family suffers with headache.

Examination —Weight, 152 pounds, height, 64 inches, span,

67 inches Lower extremities, 31½ inches, torso, 32½ inches. Circumference of head, 32½ inches, of neck, 15½ inches, of chest, 35½ inches, of abdomen, 35½ inches, of buttocks, 36½ inches Pulse, 80 Blood-pressure, 105/70

The patient is a rather broad, coarse featured, stout, middle-aged man. The skin shows an eczematous rash over the chest. There is a slight tache surrounded by a white area, no definite Sergeant's line. There is no pigmentation, the skin is smooth, soft, rather oily, not tense, with a good deal of subcutaneous fat.

Hair distribution. The scalp is covered by brown hair, medium anterior attachment, with a bald area extending upward on either side of the temples. The eyebrows are long and bushy. The beard is rather thick. (He shaves twice a week.) There is a slight tuft of hair over the ensiform and slight hair over the lower part of the abdomen below the navel. The pubic hair, however, is feminine. There are some few downy hairs over the forearms and lumbar regions, with extensive hairiness over both legs.

The face is broad and coarse, adipose, plethoric, and the skin of the face is oily and coarse. The forehead is narrow, rather broad, and receding. The nose is straight, with broad, soft tip. The eyes are hazel colored. There is slight edema of the lower lids. The pupils are round, equal, and react to light and accommodation. There is no nystagmus. Gräfe, Stellwag, Mobius, and Dalrymple signs are all negative. The ears are large, the lobules are attached.

The teeth. The left upper second bicuspid is missing, otherwise they are in good condition, slight pyorrhea in the lower teeth, the upper centrals are broad, with marked interdental spacing, the upper laterals are broad, with similar spacing. The lower centrals are also broad, with increased spacing. The dental arch is wide, the palate arch is shallow, with a thick palatal ridge.

The throat is congested, the tonsils are absent (not removed), the neck is short and broad, there are no supraclavicular fat pads, the thyroid is palpable, but not enlarged.

The chest is broad, the costal angle is very wide, with a palpable ensiform. The breasts are evidently slightly enlarged. The lungs and heart are normal.

The abdomen is markedly distended. There is slight tenderness on pressure in the epigastrium. The liver and spleen are not enlarged and the kidneys are not palpable.

The general configuration of the patient is of the masculine type, with a rather broad pelvis, with an epigastric and inguinal adiposity. He has large external hemorrhoids. The upper extremities are rather thin, the hands are wide, the fingers are square and of medium length. The lower extremities. He has no knock-knee, there is cyanosis around both knees, musculature of the lower extremities is well marked. The genitals are normal.

The urine examination was normal, the basal metabolism was +6 per cent.

The roentgenogram of the sella turcica showed no enlargement or erosion of the sella, with very irregular posterior clinoids.

The perimetric reading showed no change in the visual field.

This patient complained chiefly of weakness, periodic supra-orbital and bitemporal headaches, with an initial fainting attack, and attacks of dizziness occurring in association with the headaches.

The physical examination indicates a type of patient with distinct pituitary markings characterized by the coarse broad features, the prominent supra-orbital ridges, the broad face, the increased interdental spacing, the epigastric and inguinal adiposity, and the impotency.

The patient was put on pituitary extract, 0.15 gm. He returned two weeks later stating that he had been entirely free from headaches, that his weakness has disappeared, but that there has been no change in his sexual function. He is still on pituitary feeding, is entirely free from headaches at the present writing, but is still impotent.

Case VII Pituitary Headache Not Responding to Treatment.—R. L. A married woman of thirty-eight was referred

by Dr A E Jaffin, complaining of headaches of thirteen years' duration

Ever since childhood she remembers having headaches Her mother told her that she would get spells of temporary blindness and dizziness during the attacks of headache She remembers when going to school that she would get headaches during which her vision would become blurred and visions as of flowers would appear But these conditions did not occur during the time of the headache The headaches were mild in character until about thirteen years ago, when they became very severe Since then they have grown very much worse

The headaches begin over the glabella of the nose, extend over the frontal region of the skull, over the top of the head to the left temporal region, where they remain They are periodic and occur during the day or night, usually preceded by visions of flowers, and at times by temporary, momentary blindness They last for a day and she feels very much exhausted following the headaches She passes urine very frequently during the headaches, although she is not unusually thirsty at that time When the illness began the headaches would occur every month, but recently their frequency has gradually increased from every two weeks to every ten days, and now she gets attacks almost every day and they are much more severe She has grown very much stouter The only time when her headaches disappear is during pregnancy, usually from the time when she begins to feel life to the termination of the pregnancy, when the headaches return immediately

From the beginning of pregnancy until she feels life she usually feels much worse The headaches are more frequent and more severe She feels drowsy She vomits continually, she has no appetite and she loses in weight, but when she begins to feel life she is entirely well She is free from headaches and is energetic, also appears to be younger

About a year ago she was constantly drowsy and would remain in bed practically all the time She never perspires, but suffers from heart-burn and a peculiar burning sensation in the ears

Two and a half years ago, immediately after the birth of the last child, she had an attack of "gall-stones" characterized by epigastric pains, pain in the back, though not radiating to the shoulder or accompanied by jaundice. A year before that she had an attack of gastric symptoms which she thought might be due to numerous headache medicines she had been taking for several years without relief.

Seven days after this attack of "gall-stones" she was operated upon, the gall-bladder was removed, and it contained gall-stones and pus. Since the operation she has felt worse and the headaches have increased in severity. She has been growing much stouter, and the stouter she gets, the worse her headaches become. Her appetite is unusually hearty, she always feels hungry, and her bowels are always constipated. Her eyesight has been bad, glasses have been prescribed, but her headaches have not been relieved. She is not a very nervous woman and is of a calm, quiet disposition.

Her childhood was relatively free from the usual diseases of childhood. She had no scarlet fever, diphtheria, or pneumonia. Sixteen years ago she had rheumatism involving especially the lumbar and cervical region of the spine, the wrists, hands and feet, as well as the big toe. She has had three subsequent attacks of this rheumatism. The last attack was ten years ago.

She began to menstruate at thirteen. Her menstruation was always regular, about every twenty-eight days, usually lasting three or four days, and the quantity scant. She has headaches at menstruation only occasionally. She has been married seventeen years, has had 3 children, and no miscarriages. She was unable to nurse her children because there was very little milk in her breasts. The first child was an instrumental delivery. The other labors were normal. She is unusually fond of sweets. She is not excessively thirsty.

Her father died about the age of sixty, cause unknown. He was a stout man suffering from asthma. Her mother is alive and fairly well, of the same build as the patient, and does not suffer from headaches. She has 5 brothers and 3 sisters,

the oldest brother is forty, tall, and of the same stature as the patient. The younger brother is about three years younger than the patient, is very big and muscular, the oldest sister is forty-six, suffers from rheumatism, but has no headaches.

Examination—Weight, 188½ pounds, height, 61 inches, span, 58 inches. Lower extremities, 27½ inches, torso, 33½ inches, pelvis, 12 x 9½ inches. Pulse, 86. Blood-pressure, 115/70.

The patient is a rather stout woman, of middle age. She has a marked adiposity in the epigastrium and in the lower inguinal region of the abdomen. Her features are large and broad and acromegalic in type. No rash on the skin other than an occasional acne spot over the back. There is an area of pigmentation over the chest anteriorly and posteriorly, outlining the border of a bathing suit and is probably due to sunburn. Her skin is smooth and soft, not tense.

Hair distribution. The scalp is covered by abundant hair, mostly dark in color, but with occasional gray streaks. The eyebrows are thin, slight hair in front of the ears. There is marked absence of hair over the forearms and legs. The pubic hair is of the feminine type. The axillary hair is marked.

The face shows slight asymmetry, the right side being more evident than the left, and there is a slight weakness of the left side of the face which the patient says she has only noticed this summer. The forehead is broad, the supra-orbital regions are not prominent, the glabella is wide, the eyelashes are long. There is no edema of the eyelids. There is no exophthalmos. The palpebral fissures are of medium width, there is no nystagmus. The pupils react to light and accommodation. Gräfe, Stellwag, Kocher, Mobius, and Dalrymple signs are negative. The ears are rather flat, somewhat congested, oily, and the lobes are attached. The examination of the auditory canal shows a normal tympanic membrane. The nose is rather broad, short, soft tip, the intranasal examination shows no evidence of pathology.

Teeth. The upper front and left incisors are absent, the right upper lateral incisor is large and normal, the canines are blunt. The lower teeth are in good condition.

There is a slight prognathism of the lower jaw. The palate is highly arched, the dental arch is wide. The tonsils are submerged but moderately enlarged. The voice is of a basso quality. The neck is rather short with marked adiposity, the thyroid is palpable, but not enlarged.

The chest is broad, the costal angle is wide, the ensiform is palpable. The breasts are large and pendulous, the nipples are slightly prominent. The lungs and heart are normal. There is no evidence of arterial weakness in any of the visible or palpable vessels.

The abdomen is pendulous, there is an oblique laparotomy scar in the right upper quadrant of the abdomen. No areas of tenderness or rigidity. The lower border of the stomach is felt about two fingerbreadths below the level of the navel. There is tenderness in the left lower quadrant of the abdomen. The liver and spleen are not enlarged. The kidneys are not palpable. The upper extremities are rather large. The hands are rather broad, the fingers are short and square. The lower extremities are adipose, no edema, and no hairiness present. Urine examination was negative. The basal metabolism showed +19.6 per cent. The Goetsch test was negative and a pilocarpin test was moderately positive.

The perimetric readings showed no change in the visual field. The x-ray examination showed a small sella turcica with a blunt anterior clinoid and an indefinite outline and cloudiness of the right frontal sinus.

This patient is suffering from periodic headaches which she has had since childhood and which have recently been growing worse. The fact that they are periodic in character, that they are accompanied by attacks of blurring in vision, and that the only time when they are absent is during the latter half of pregnancy, indicates that they are of the distinct pituitary type.

There is, however, a slight cloudiness of the right frontal sinus, although there has never been any evidence of sinus trouble.

Because of the fact that the headache was characteristically

pituitary in type it was decided to try organotherapy before attacking the sinus trouble. In this case there was such a distinct history of relief during pregnancy that it was suggested to try placental extract in large doses first. The patient was put on about 20 grains of placental extract a day for about a month, with absolutely no relief of the headaches. Placental extract was then stopped and she was placed on whole gland pituitary extract in gradually increasing doses until she was getting from 20 to 30 grains pituitary extract a day, but up to the present there has been no improvement in her condition.

It would seem likely, therefore, that attention to the cloudy frontal sinus might solve the difficulty. She has, however, had her headaches practically all her life. They were definitely associated with fainting spells, with blurring of vision, fatigability, etc., which seem to indicate rather that they are pituitary in character than due to the sinus trouble. There are any number of possible explanations as to why therapy has so far been futile in this case. One is that there may be actual structural changes in the pituitary or that there may be an organic lesion, in spite of the fact that there are no eye symptoms. However, further explanations would merely be mental gymnastics. The fact remains that here was a case who in spite of the very definite pituitary findings and history has not responded so far to rational therapy on that basis.

Note —The sugar tolerance was not done in any of these cases because nearly all of them had a characteristic obesity of the pituitary type. The sugar tolerance test in pituitary diseases is only of value in the absence of characteristic obesity, because it determines a mild degree of increased sugar tolerance which is not present to the extent of causing a characteristic obesity.

ADRENAL CORTEX THERAPY IN HYPERTHYROIDISM

The fundamental basis for organotherapy is a deficiency in the functional activity of one of the ductless glands. If we can recognize such a deficiency and if we have a proper preparation of the deficient gland, the administration of such a sub-

stance produces a specific curative result. Such therapy has been followed by notable success in the definitely recognized condition of thyroid deficiency, such as myxedema and frequently with similar success in the mild types of thyroid deficiency. There are many functional diseases of various viscera in which the underlying basis is a deficiency of thyroid secretion. The administration of thyroid extract to such patients brings about definite therapeutic effects. Various functional diseases of the stomach characterized by anacidity, occasionally achylia gastrica, and other conditions are frequently definitely relieved by the administration of thyroid extract when clinical or laboratory evidence of thyroid deficiency can be demonstrated.

Overactivity of the ductless glands, such as hyperthyroidism, for instance, has not heretofore responded much to organotherapy. If we look at the condition of hyperactivity alone it seems rather improbable that substitution therapy should be useful in such conditions. Looking at the problem from a biologic standpoint, it would seem rather unlikely that a disturbance in the physiology of the ductless glands, or of any organ, should result in overactivity. On the contrary, any physiologic disturbance or any disturbance in the structure or function of any organ, whether this be due to an actual injury or as the result of an infection, must result in a lessened activity of an organ. Consequently, since the ductless glands functionate as a system it seems much more probable that conditions of overactivity in the ductless glands are not the primary manifestations of the underlying disturbance.

In other words, whenever we have an overactivity of any of the ductless glands we must regard it either as an associative or a compensatory phenomenon of some structural injury, such as an infection or disturbed function, elsewhere in the endocrine chain. Thus, for example, if we have clinical evidence of hyperthyroidism this should not be considered as the primary condition. It should be regarded as merely the response either to an infection somewhere in the body in which we may consider the hyperthyroidism the clinical manifestation of the

patient's effort to overcome this infection or merely as evidence of disturbance in the endocrine system as a whole in which there is a deficiency in one or several of the other ductless glands.

The gradually accumulating evidence of endocrine physiology indicates that the endocrine system functionates as a system. When one of the glands is injured or its function eliminated or diminished, there usually develops evidence of overactivity of some other glands as well as a synergistic underactivity of different glands.

Consequently, in any condition of overactivity we must solve the problem in two ways: first, we must look for an etiologic factor such as an infection for instance, and, second, we must look for evidence of functional deficiency of some other ductless glands.

This afternoon I shall present a number of cases which demonstrate clinical evidence of deficiency of other ductless glands especially the adrenals in hyperthyroidism. Clinically it can frequently be appreciated that the hyperthyroidism is merely evidence of the patient's response to some etiologic factor such as an infection. Every once in a while a definite focal infection in the teeth and tonsils is responsible for the hyperthyroidism and a removal of these primary lesions causes a prompt improvement in the symptoms. This is not as common as one expects from the literature however.

If we are to make any progress in organotherapy in cases of hyperthyroidism our efforts should be devoted to the discovery of evidence of deficiency in other ductless glands, and to obtain proper preparations of these glands to administer on the basis of substitution therapy. Osler has always emphasized the importance of asthenia and profound weakness as an important symptom in exophthalmic goiter and hyperthyroidism. Kocher has laid stress upon the frequency with which pigmentation and asthenia occur in exophthalmic goiter and hyperthyroidism. Furthermore he has stated that the feeding of suprarenal extract causes the disappearance of the hyperthyroidism in the patient. Julius Bauer has made similar observations. G. A. Friedman in a recent article, has also

called attention to the clinical evidence of adrenal insufficiency in hyperthyroidism

A thorough examination of cases of hyperthyroidism indicates that profound asthenia is one of the most important symptoms of this condition and in many of these cases pigmentation of the skin and mucous membrane is very common and extensive. The analogy of extensive pigmentation and asthenia in hyperthyroidism with the same symptoms as those of Addison's disease has led many clinicians for the last five or ten years to believe that these symptoms occurring in hyperthyroidism were indicative of involvement of the suprarenal glands and since Addison's disease is characterized by profound asthenia by extensive pigmentation symptoms which indicate adrenal insufficiency, we have a right to believe that the same symptoms occurring in hyperthyroidism also indicate adrenal insufficiency. Furthermore it has been shown that asthenia and pigmentation, especially the latter, are due to involvement of the adrenal cortex. Consequently it is reasonable to assume that a deficiency of the adrenal cortex exists in hyperthyroidism.

Since disturbances in physiology must result primarily in diminution or deficiency in function it seems likely that deficient function of the adrenal cortex is probably the primary factor in hyperthyroidism. Recently Marine and Bauman have attacked this problem experimentally. They were able to produce a condition of hyperthyroidism in animals characterized by an increased basal metabolism by freezing the adrenal cortex.

On this basis we have been treating cases of hyperthyroidism at our endocrine clinic for the last two years. The results are not always constant and we are still investigating the problem and I hope shortly to present a large series of cases so treated. We have obtained definite information as to the effects of this remedy in the cases treated. The adrenal cortex that we use was freshly desiccated adrenal glands obtained from the ox, which is administered in capsule form. The evidence seems to show that definite effects can be obtained from this remedy in a short time.

The objective symptoms disappear before subjective improvement takes place. The first notable effect is a gain in weight and a lessening of the asthenia. This is followed by a slowing in pulse-rate, a diminution of the nervousness, and a reduction in blood-pressure, and by a reduction in the basal metabolic rate. In some instances simultaneously and in others later the subjective symptoms have improved. We have also used this substance in cases of gastric neuroses characterized by hyperthyroidism as indicated by the clinical evidence and by the basal metabolic rate.

I do not mean to indicate that this form of therapy is the only therapy for hyperthyroidism, but it seems to me that progress along this line will ultimately develop a specific for hyperthyroidism.

The improvement in our cases has been especially noteworthy, as the treatment has been used principally on ambulatory patients without the use of any other remedies.

Case I. Exophthalmic Goiter—E. R. A young married woman of thirty-six came under observation on March 22, 1921 complaining chiefly of nervousness, palpitation of the heart, and enlargement of the thyroid gland.

She was perfectly well until about a year ago. At that time she noticed an enlargement of the thyroid gland. This was associated with palpitation of the heart and with extreme nervousness. For the last eight months she has noticed a gradually increasing bulging of the eyes. She has pains in the knees, the shoulders, and the lumbar spine. She has shortness of breath on exertion and develops precordial pain at that time. She has lost about 20 pounds in weight. She has occasional burning pain immediately after eating, with an occasional nausea, but no vomiting. Her bowels are constipated. She has profound asthenia and gets tired so easily that she is unable to do her housework. She has occipital headache, but the headache is not characteristically of the pituitary type. She perspires very freely.

She had influenza in childhood. She had no measles, but

had scrofula with a peculiar rash on the head in childhood. She had an appendix operation three or four years ago.

She began to menstruate at the age of sixteen. In the beginning her menstruation was irregular, she had amenorrhea for the first nine months. Her menstruation usually lasts seven days. It is scant and she has very little pain, although she has slight headache at that time, not pituitary in character. She has been married eleven years and has had 3 children, one child died of status lymphaticus. The other children are not well, one suffers from rheumatism, the other has a running ear.

She is very fond of sweets and drinks coffee moderately.

Her mother died of heart disease, her father is alive and well. She has 3 sisters living, one sister has goiter and asthma.

Examination—The patient is a rather thin, nervous woman, weighing 125 pounds and 62½ inches in height. There is no rash on the skin other than a slight eczema on the upper lip and slight acne on the back. There is no Sergent's line, but there is a marked tache. The skin is smooth, oily, rather moist, and tense.

Hair distribution The scalp is covered by abundant coarse dark brown hair with medium anterior attachment. There is hair on the body and she has fine downy hair on the forearms and legs. The axillary hair is marked. The pubic hair is of the feminine type. There are very many brown pigmented spots over the chest and back and many freckles on the face. The head is rather broad. There are no prominent supra-orbital ridges. The nose is smooth, broad, and straight, with a soft tip. The mouth. The teeth are in poor condition, the upper set are mostly gone and replaced by a false set. The tonsils are large. There is no evidence of infection. The throat is moderately congested. The eyes show a marked exophthalmos. Graefe, Stellwag, and Mobius signs are all positive. The pupils are round, equal, and react to light and accommodation. There is no nystagmus. The neck shows a marked enlargement of the thyroid gland, and measures 16½ inches in circumference.

The chest is narrow, the costal angle is of medium width,

the ensiform is not palpable. The breasts are large and well developed. The lungs are normal, the heart is not enlarged, there are no murmurs, but it is rapid. The pulse is 128 and the blood-pressure is 175/95.

The abdomen is not distended. There are no areas of tenderness or rigidity. There are no abnormal masses to be felt. The liver and spleen are not enlarged. The kidneys are not palpable. The lower border of the stomach extends to the level of the iliac crests. The upper extremities are thin. The hands are narrow, the fingers are long, the hands are moist. The lower extremities show nothing abnormal. The urine examination was normal. The roentgenogram of the sella turcica showed no changes. The basal metabolism showed $+62\frac{1}{2}$ per cent.

This patient was a classical hyperthyroidism. There was no evidence of any focal infection in her tonsils or teeth. She was placed on adrenal cortex, 0.06 gm. three times a day, and was kept on that steadily, gradually increasing to 0.12 gm. three times a day. She began to improve about four weeks after the first observation, gaining at the rate of about 2 pounds a month for the first three months, and then about a pound a month, and her nervousness cleared up.

In October, 1921 she weighed 134 pounds. Her blood-pressure was 160/100 and her pulse was 118. The dose of the adrenal cortex was now increased.

In December, 1921 her blood-pressure was 140, her weight was 139 pounds, her pulse was 112. The exophthalmos had practically disappeared.

On January 24, 1922 her weight was 140 pounds, her pulse 104, her blood-pressure 124/96, her thyroid measured 15 inches, and she is entirely free from symptoms.

Her basal metabolism is now $+16$ per cent.

Case II Hyperthyroidism C. B. A married woman thirty-nine years of age came under observation in October, 1921. She complained chiefly of enlargement of the thyroid gland, nervousness, and palpitation of the heart. For the last six weeks has noticed enlargement of the thyroid gland. She has grown quite nervous. The illness began with a sudden

shock resulting from one of her children falling down stairs and injuring herself. She was quite nervous before that, but she has gradually grown worse. She has also developed palpitation of the heart. She has not noticed any exophthalmos, although it is evident. She does not seem to have lost in weight, although she thinks she has lost about 3 or 4 pounds. She has no gastric symptoms, she gets tremors in the legs and has profound weakness. She has no headaches. She perspires very freely. She has very excessive thirst. Her appetite is good. Her bowels move regularly. Her menstruation began at thirteen, it was always regular and quite profuse. She has pain occasionally and rarely headache. She has been married twenty years, has had 14 children, 9 of whom are living and 5 have died.

Her father died of heart trouble, her mother of pneumonia and grip. She has one sister and one brother, younger than herself. No history of goiter or diabetes in the family.

Examination—Weight, 104 pounds, height, 60½ inches, span 61½ inches. Lower extremities, 32½ inches, torso, 28 inches. Pulse, 135. Blood-pressure, 170/90.

The patient is a rather thin, apprehensive, nervous woman. There is no rash on the skin, but there is marked brownish pigmentation over the buttocks, forearms, abdomen and neck. The skin is moist, tense, smooth, and there is a marked absence of subcutaneous fat.

Hair distribution. The scalp is covered by an abundant, fine silky white hair (the hair has been white for fifteen years). There is no hair on the body, the pubic hair is of the marked feminine type, the axillary hair is extensive. No hairiness of the forearms and legs.

There is marked tache but no Sergeant's line. The head is rather large, the forehead is straight, with no prominent supra-orbital regions. The face is rather thin, narrow, and oval. There is a moderate enlargement of the thyroid gland. The features are well developed, the nose is straight and thin, the glabella is narrow. There is a moderate exophthalmos. Graefe, Stellwag and Mobius signs are positive. The pupils

are round, equal, and they react to light and accommodation
There is no nystagmus

The teeth are in poor condition, markedly pigmented, with carious condition in the upper front teeth and pyorrhea. The tonsils are large. The circumference of the neck is $14\frac{1}{2}$ inches. The chest is rather narrow, breasts are of moderate size and well developed, rather pendulous, the lungs and heart are normal except for the tachycardia noted. The abdomen is soft and flabby. There are no areas of tenderness or rigidity present, the liver and spleen are not enlarged, the kidneys not palpable. The abdominal wall is flabby. The upper extremities are thin, the hands are moist, and there is a fine tremor of both hands. The lower extremities are thin and show nothing abnormal. The urine examination was negative. The roentgenogram of the sella turcica was normal. The basal metabolism showed +55 per cent.

This patient was a clinical case of hyperthyroidism which evidently came on in a woman with a dominant thyroid physiology. She was always thin, she was always nervous. She was very active sexually and very prolific. The sudden shock of the injury of her child was what probably initiated the thyroid overactivity. Hyperthyroidism and exophthalmic goiter are extremely common among patients who are considered as thyroid dominant type. In other words, the slightest mental shock or infection reacts upon their thyroid, producing the hyperthyroidism.

She was placed upon adrenal cortex, 0.06 gm. three times a day, to test the value of the remedy before attempting to put her teeth in condition. She came in a month later, stating that her nervousness was very much better, the exophthalmos had gradually diminished, her pulse was 120, and the blood-pressure was 104/75. She weighed 107 pounds.

She did not return until the early part of January, 1922. She now weighs 112 pounds, her pulse varies between 70 and 80, and her blood-pressure is now 135/60. The neck circumference is 11 inches. Her basal metabolism is +23 per cent.

Case III Hyperthyroidism with Dominant Gastric Symptoms—I S A young married woman of thirty-four came under observation in the latter part of November, 1921, complaining chiefly of constipation of fifteen years' duration, with an enlargement of the neck of two months' duration

For the last fifteen years the patient has been constipated. She is easily excited and she always has an uncomfortable feeling in the stomach, which is worse when she is excited. For the last two months she has noticed an enlargement of the thyroid gland which has gradually grown larger. She has become intensely nervous, is unable to concentrate, and is very fidgety. She has palpitation of the heart on the slightest exertion. She has a profound weakness which is so marked that she is unable to do the simplest housework. She gets attacks of crying spells. She has lost about 8 pounds in weight since the onset of her trouble, she has no headaches, no excessive perspiration, but her tongue feels large and seems to burn, and her mouth is constantly dry. She has pain in the epigastrium after eating.

She had scarlet fever at the age of nine, which was complicated by a broken-down abscess in the neck. She had an acute infection, which evidently was malaria, at the age of twelve. She had influenza two years ago without any complications except a feeling of profound weakness. She was never operated upon except for a vaginal tear after a childbirth. She has no unusual food likings, does not drink coffee or tea, her appetite is good.

Her menstruation began at thirteen, somewhat irregular, that is, it comes a few days early, she has no pains, but an excessive flow, about seven days. She has been married eleven years, she has 6 children, one is nine years, twins of seven years, one of five and a half years, one of four years, and one of ten months. She had one miscarriage soon after marriage. During her menstrual period she becomes very nervous, she has no headaches. During pregnancy she feels very well.

Her father is well, her mother committed suicide and was very nervous. She has 2 sisters and 2 brothers, all of whom

are very thin and highly nervous. There is no goiter, diabetes, or other constitutional disease in the family.

Examination—Weight, 124 pounds, height, 62½ inches, span, 62 inches. Lower extremities, 33½ inches, torso, 29 inches, pelvis, 11½ x 8 inches. Blood-pressure, 145/95. Pulse 122.

The patient is a fairly well-developed, rather tall, thin, highly nervous, and apprehensive young woman. Her skin is soft, oily, rather dry. There is marked pigmentation over the chest, back, and over the abdomen.

Hair distribution. The scalp is covered by long, fine, straight, silky hair, with marked anterior attachment. The eyebrows are rather thick, with a few hairs over the glabella. There are a few scant hairs over the forearms and marked absence over the legs. The pubic hair is feminine.

The forehead is narrow, straight. The nose is long, rather thin, with a soft tip. There is a moderate exophthalmos. The Graefe, Stellwag, and Mobius signs are positive. The eyes are brown, the pupils are round, equal, and react to light and accommodation. The ears are flat, the lobes unattached. The teeth. The upper set are gone and have been replaced by a complete false set, the lower show marked pigmentation, but no purulent secretion, the tonsils are enlarged. The neck is long, the thyroid is moderately enlarged, the circumference is 14½ inches.

The chest is rather narrow, the breasts are small with prominent nipples, with extensive pigmentation. The lungs are normal, the heart is rapid, the rate is 122.

The abdominal wall is pendulous. There are no masses, no rigidity, there is marked tenderness on pressure in the epigastrium. The right kidney is movable. The extremities. The upper extremities are thin, narrow, the hands are moist showing a fine tremor. The lower extremities show marked varicose veins, no edema. Vaginal examination shows a cystocele and rectocele, with slight laceration of the cervix. The urine examination was normal. The analysis of the gastric contents showed a free acidity of 62. The basal metabolism showed +48 per cent.

This patient gave evidence of hyperthyroidism in which the constipation and gastric symptoms preceded the onset of the enlargement of the thyroid gland. She was placed on adrenal cortex, 0.06 gm three times a day. She was seen again on January 3, 1922. Her blood-pressure at this time was 132/84. Her weight was 127½ pounds. She had a pulse of 92. She was much quieter, her gastric symptoms have subsided, and her constipation has improved.

She was seen again on January 24, 1922. Her weight was 128½ pounds, pulse 84, blood-pressure 110/86, and she was entirely free from symptoms.

On January 31, 1922 she weighed 130½ pounds. The nervousness was gone, her blood-pressure was 110/86, her pulse 72. The adrenal cortex was increased to 0.2 gm three times a day.

The enlarged thyroid had almost completely subsided. This patient showed a condition of hyperthyroidism, with dominant gastric symptoms, which was relieved by the administration of adrenal cortex. She is an ambulatory patient without any other treatment.

Case IV Essential Hypertension in a Boy with Evidence of Hyperthyroidism—L. P. A young boy of sixteen was referred by Dr. A. E. Jaffin, of Jersey City, complaining of palpitation of the heart and nervousness. He was well until ten months ago, when his father died of pneumonia. Since that time he has been growing exceedingly nervous, has developed palpitation of the heart, and rather indefinite pains in the back of the chest. He does not cough. He is constantly downhearted and cannot concentrate, and he has tremors of the hands. He does not perspire excessively. Since the onset of his trouble he has lost 35 pounds in weight. He has no headaches. He had measles and chickenpox in childhood. He had a "touch of pneumonia" at the age of two. He is very fond of sugar and spicy substances. He frequently has epigastric pain after eating, with occasional nausea. He has profound weakness and gets exhausted very easily.

His father died of pneumonia at the onset of the illness. His mother is alive, thirty-six years of age. About eight years

ago she had enlargement of the thyroid gland, but it disappeared after massage

Examination —Weight, 143 pounds, height, 68½ inches, span, 68 inches Lower extremities, 36 inches, torso, 32½ inches Blood-pressure, 175/90 Pulse, 138

The patient is a rather tall, thin young man The skin is smooth, rather tense, with marked absence of subcutaneous fat There is a definite tache, but a suggestive Sergeant's line There is light lanugo-like hair over the upper lip and on the side of both cheeks There is a slight growth of hair over the thighs and legs and slightly over the forearms and abdomen The pubic hair is of the feminine type The scalp is covered with abundant thick, dark, curly hair, which is attached with a medium anterior attachment The forehead is broad, straight, the eyebrows are not unusually thick The palpebral orifice is of medium width The eyes are brown, the pupils are round, small, equal, and react to light and accommodation The nose is straight, with a soft tip The upper front incisors are replaced by bridgework The lower set is in good condition The canines are long and the upper lateral incisors are narrow The x-ray of the teeth showed a slight apical absorption of the second bicuspid The dental arch is of medium width and the palatal arch is high The throat is congested, the tonsils are slightly enlarged The neck is long, the thyroid is not enlarged, but palpable There is no supraclavicular adiposity The chest is of medium width, the costal angle is a right angle The ensiform is not palpable, the lungs are normal, the heart is not enlarged, there is marked tachycardia, and a slight accentuation of the second aortic sound

The abdomen is not distended There is slight tenderness on pressure in the epigastrium The lower border of the stomach extends to about a fingerbreadth below the level of the navel The liver and spleen are not enlarged The kidneys are not palpable The pelvis is very broad (11 x 7½ inches) The genitals are normal The extremities show slight cyanosis of the hands, which are moist There is a marked fine tremor of both hands The lower extremities show no edema, and only the hairiness

above noted The urine examination was negative The roentgenogram of the sella turcica showed nothing abnormal The basal metabolism showed +44 per cent

This patient came under observation December 10, 1920 He came under observation on account of nervousness, palpitation of the heart, tremors, and indefinite pains, following the death of his father The examination showed only clinical evidence of hyperthyroidism without exophthalmos, without enlargement of the thyroid gland, but with marked tremors, tache, slight gastric symptoms, and an increased basal metabolism, with evidence of hypertension 175/90 This hypertension was considered to be the dominant factor, and since there was no evidence of cardiovascular or renal disease, the diagnosis was believed to be essential hypertension

The patient was put on adrenal cortex, 0.06 gm three times a day This was increased to 0.2 gm three times a day He returned again on March 11, 1921, with a blood-pressure of 115/70, pulse 118 The weight was 149 pounds

On May 27, 1921 the weight was 152 pounds, blood-pressure 135/70 The tremor was gone The pains and nervousness were all gone The patient's basal metabolism at this time was +28 per cent

On August 25, 1921 the blood-pressure was 126/68, the pulse 108 The weight was 152 pounds

On October 14, 1921 the blood-pressure was 130/90, weight 151 pounds, pulse 82 At this time it was noted that there was a beginning growth of hair over the chest, both breasts, upper part of the abdomen, shoulders, and lumbar region All symptoms were gone

On November 18, 1921 blood-pressure was 140/80, pulse 98, weight 151 pounds He worries a good deal because business is bad

On December 23, 1921 blood-pressure was 125/75, pulse 84, weight 150 pounds No symptoms, feels entirely well

The last observation was on January 27, 1922 blood-pressure 130/75, pulse 78, weight 152 pounds No symptoms

Basal metabolism +15 per cent. Feels much better and stronger

This patient is a young boy suffering from hypertension. There was no evidence of any cardiac, vascular, or renal disease. It was therefore considered as a case of essential hypertension. Because of the tachycardia, the tremors, the nervousness, and the increased metabolic rate hyperthyroidism was believed to be the basic cause. On this basis he was treated with adrenal cortex, beginning with 0.06 gm. and increasing up to 0.2 or 0.25 gm. taken repeatedly, with the result that there was a gradual reduction in the hypertension with an improvement in the hyperthyroidism. An interesting point worthy of note in this case was the presence of the feminine pubic hair and very broad pelvis in his constitutional make-up. This is worth noting to determine whether the feminine constitutional make-up has anything to do with the greater frequency of hyperthyroidism in females than in males.

This patient was observed for quite a long time, but we must be guarded in drawing conclusions. It is quite likely that the therapy had nothing to do with the improvement of his condition. This may have been due to the adjustment of the basic emotional factors in his life quite apart from the therapy. At any rate, the associated hyperthyroidism was improved. Extensive investigations along this line are being carried out in our clinic.

CLINIC OF DR ALBERT A EPSTEIN

MT SINAI HOSPITAL

CLINICAL COURSE AND THERAPEUTIC MANAGEMENT OF CHRONIC NEPHROSIS

IN a previous contribution¹ I have attempted to describe the various clinical types of chronic parenchymatous nephritis. Among the varieties presented there was one which differed from the others in many important respects, and to which the term "chronic nephrosis" was applied. This type we shall consider now, more particularly from the standpoint of its clinical course and therapeutic management.

Before proceeding with our cases, however, it may not be amiss to state briefly the probable nature of this malady. Thus I deem necessary, because of the evident confusion that still exists in the minds of many concerning it.

Because of the striking urinary disturbances which accompany this disease the belief is current that it is primarily and essentially a renal disease. This belief is deeply rooted, although based on a misconception, namely, that the renal condition constitutes the "whole" disease. Close analysis favors the view that the renal disturbance in this disease is but one of a number of phenomena due to a common cause, namely, a systemic disorder of a metabolic character.

What is chronic nephrosis? How does it arise? Whom does it affect? What are the clinical and pathologic characteristics which distinguish it from all true kidney affections?

It is fair to admit that absolute standards for the differentiation of chronic nephrosis from the other types of "chronic parenchymatous nephritis" are still lacking, and it may at times be impossible to definitely place a given case. However, the

disease possesses certain distinguishing features. I shall not enter into a discussion of all of these now, they have been amply discussed in the contribution to which I have already referred. It is important to remember that it occurs in relatively young individuals and is not at all uncommon in children. It is presumably of unknown origin, and it bears no definite relationship to infectious diseases. Three facts stand out prominently in respect to its etiology: (1) Its incidence is greatest among the poor, (2) it occasionally develops in the course of or after a pregnancy, and (3) it occurs in association with hypothyroid states. Whether the causative agency has a common basis in all of these is not certain. Its incidence among the poor suggests its relationship to defective nutrition, whereas its occurrence in association with pregnancy and hypothyroid states places its etiology in the realm of endocrine disorders. There is much evidence to support these suppositions, and we shall consider them in the discussion of our cases.

The lack of definite knowledge of the pathology of chronic nephrosis has added to the existing confusion concerning this disease. If we may place the pathologic processes in two categories, (1) general or systemic and (2) local or renal, we may clarify the situation considerably.

Of the general systemic conditions which characterize this disease the most important ones are the changes in the blood, the edema, the albuminuria, and the change in the basal metabolism. The changes in the blood are characteristic of this disease and consist in an increase in the lipid content of the blood, in a decrease of the protein of the blood serum, and in the alteration or inversion of the normal albumin-globulin ratio. Normally the cholesterol content of the blood varies from about 0.175 to 0.225 per cent. Although slight variations occur in other diseases, the most marked increase occurs in chronic nephrosis. In my cases I have found figures varying from 0.300 to 1.300 per cent. I consider this increase of fundamental importance. This increase has since been noted by other observers, and the fact that the serum of certain nephritics may give a milky appearance has been observed by the older writers on nephritis.

The reduction of the protein in the blood-serum is just as characteristic. Normally this forms about 6 to 8 per cent, and the ratio of albumin to globulin is approximately 2 to 1, the globulin forming about 37 per cent of the total protein. In chronic nephrosis I have found the total protein of the blood-serum to be greatly reduced and to average 3.928 per cent, and the ratio of albumin to globulin to average 0.466 per cent of albumin to 3.426 per cent of globulin, the globulin thus forming 89.2 per cent of the total protein.

This loss of protein is important, as it stands in direct relationship to the next important pathologic condition mentioned, namely, the edema.

It is not necessary to undertake here a lengthy discussion of edema. I have discussed it sufficiently in a previous publication² and shall mention here only the essential points in my conception of edema in chronic nephrosis as they bear on the subject at hand. Normally there is a nice balance maintained in the fluid interchange between the blood and the tissues, varying with the activity and the demand of the tissues. The forces maintaining this balance are, on the one hand, the intracapillary pressure, and on the other, the osmotic force of the proteins and other dissolved substances in the blood. In other forms of edema, such as those of cardiac origin, it is the increase in the intracapillary pressure which is the immediate cause of the edema. In edema of chronic nephrosis it is the change in the osmotic force of the blood which is the direct cause.

Starling has shown that the proteins of the blood exert an osmotic pressure of 25 to 30 mm of mercury. It can be easily seen that the loss of protein as given in the above figures represents a loss in the osmotic force of the blood, often to more than half. This diminution in the osmotic force causes a marked disturbance in the balance, and not only favors the passage of fluid from the blood to the tissues, but gives to the tissues the controlling power to absorb and retain fluids.

Support to the explanation has been given by the studies in war edema, in which several observers have noted a considerable diminution of protein in the blood-serum, and also

by the experimental production of edema by protein under-nutrition

The edema is general and may be very marked. Effusion occurs in all serous cavities. The edema of the face gives in the adult a peculiar grayish-white appearance to the skin, in the child the skin assumes a bluish-white hue, like that of dilute milk, although the examination of the blood does not show any or only a very slight anemia.

You have noticed that I have classified the albuminuria under the heading of general systemic conditions. Albumin in the urine has been the one symptom considered as indicative of renal disease. With the increase in knowledge concerning the disease under discussion it has become more and more evident that the albuminuria of chronic nephrosis is not of a purely local or renal origin, but is the result of a profound general metabolic change. I shall return to this question later.

The one other important change that I mentioned above is the decrease in basal metabolism. I have noticed long ago the close resemblance of this disease to certain mild forms of myxedema and also the beneficial effect of thyroid administration thereon. Dr. Lande and myself² have carried out a series of studies in basal metabolism in cases of chronic nephrosis, these form the subject of another report. We have found invariably a decrease in the basal metabolism, at times as much as 30 per cent below normal. I am convinced that there are borderline cases, on the one side of which there are the cases of chronic nephrosis and on the other side cases of hypothyroidism and fruste forms of myxedema.

As I have stated before, the renal pathology of this disease is still not fully settled. Those who have had occasion to study the kidneys of such cases (Fahr, Munk) give the following description. The kidney is enlarged, soft, smooth, and of a yellowish-white color. The capsule strips easily. On the cut surface the cortex and medulla contrast sharply, the cortex has a yellowish-white appearance and small yellowish-gray dots may be visible. Microscopically there are found changes in the primary convoluted tubules. Fatty degeneration is the

dominant lesion, although here and there albuminoid degeneration may be found. The cells are filled with small and large fatty droplets, among which double refractive lipoids, such as cholesterol, predominates. The secondary convoluted tubules are only very slightly affected, while the ascending and descending arm and the loop of Henle are not at all affected. The glomeruli are not affected and only occasionally show a fine sprinkling of fatty droplets. Lipoid deposit is also found in the interstitial tissue with a consequent small cell infiltration. The lumen of the tubules contains casts of albumin and tubular cells containing lipoid. Regeneration of tubules can be seen here and there.

The kidney evidently participates in the general change due to the increase of lipoids in the blood. It may be of interest in this connection to add that Kaethe Dewey⁴ produced a lesion very much like the above by the infusion of cholesterol emulsion into the blood-stream.

The pathologic condition as here described differs from the cases of nephrosis of known etiology, such as that due to tuberculosis, lues, and the amyloid kidney. It also differs from the cases of acute nephrosis which are due to bichlorid of mercury poisoning, diphtheria, etc. I question seriously the existence of any cases of *chronic nephrosis* which are the outcome of *acute nephrosis*.

We have here, therefore, a disease of gradual onset, chronic cause, characterized by edema, anasarca, and effusion in the serous cavities, by a marked albuminuria, with or without casts, and the absence of any blood in the urine, by the absence of hypertension and cardiac hypertrophy, characterized by a reduction in the protein content of the blood, inversion of the albumin-globulin ratio, and by the increase in the blood lipoids, and finally, by a reduction in basal metabolism.

Because of the confusion referred to above, we have been slow in the acquisition of knowledge concerning this disease. But I believe we have reached a stage where we can formulate our conception of chronic nephrosis. Let us return to the albuminuria. We have seen that the loss of albumin through

the urine is enormous, just as is often the loss of sugar in diabetes mellitus. How shall we explain the loss? The answer that the kidney cells become permeable to protein is a very hypothetical one, has never been substantiated, and does not add anything to our understanding of the disease. My conception of the albuminuria is that it is the result of an *active excretion* of serum protein by the kidney. Because of the change in the protein (chemical, physical, or biologic), as a result of which the body is unable to utilize it for whatever function the protein serves, it is excreted by the kidney as a foreign substance, just as the kidney excretes any other foreign substance injected into the blood-stream. The change implied is a qualitative one,* although adequate means are still lacking to determine its nature. The quantitative changes in the serum protein which we do find are the result of the drain on the blood-serum caused by the albuminuria.

We are here, therefore, face to face with a condition which is really a general metabolic disorder. The term "nephrosis" is misleading in so far as it puts all the blame on the kidney, which is only of secondary importance in this disease. Proper terminology adds to the clarity of our conceptions. Just as in diabetes mellitus we have a glycosuria and back of this a perversion in carbohydrate metabolism, so in this disease we have an albuminuria and back of this a perversion in protein metabolism. It would be far more appropriate to designate this disease as a "diabetes albuminuricus."

The importance of the conception outlined above is at once evident when we come to the treatment of this disease. Our objective here is threefold: (1) To replace as much as

* The chemical methods of analysis are as yet too crude to determine the fine changes that take place in the blood serum in response to various causes. That such changes do occur is certain. This fact is amply illustrated by the various immunochemical changes which result from infectious diseases and different immunologic processes. Another excellent illustration of the above conceptions is furnished by the comparison of blood sera of different origins. Chemically the blood serum of one species of animal may be exactly like that of another, yet when introduced into the blood stream of the second species may produce very striking toxic phenomena.

possible the protein lost from the blood, (2) to compel the tissues to utilize the lipid accumulation in the blood, and (3) to re-establish normal metabolism. These requirements are best fulfilled by feeding the patients the high protein, fat-free diet which I introduced several years ago.

Briefly the diet is as follows. Protein foods, preferably those free from fats and lipoids, such as whites of eggs, washed casein, oysters, lean fish, and the like are given in amounts sufficient to make $1\frac{1}{2}$ to 2 grams per kilo of body weight. In certain instances the quantity of protein allowed may be as high as $2\frac{1}{2}$ to 3 grams per kilo of body weight. The fat is entirely excluded from the diet as long as the lipoidemia persists. When it subsides, lipid-containing protein foods of animal origin are allowed, such as beef, ham, chicken, etc. The amount of carbohydrate allowed is somewhat variable, depending largely on the appetite of the patient. Essentially the diet is a high protein, low calory diet. Its aim is, first, to replace the protein loss and, second, by virtue of its low caloric value, to compel utilization of protein. There is no special limitation on the amount of salt, enough being given to make the food palatable without any undue excess. Sufficient fluids are allowed to prevent the patient from suffering unduly from thirst.

In certain cases the high protein diet accomplishes all that is required of it, in certain other cases it stops short of a complete cure. In these cases the addition of thyroid therapy will accomplish this result. There are still other cases in which the protein therapy will not produce any effect until thyroid is administered. It is often necessary, however, to give the thyroid in increasing doses until a definite effect is produced. In certain instances the tolerance for thyroid extract is quite remarkable and very large doses are required.

I shall now proceed to illustrate by concrete examples some of the points which I have just discussed.

Case I—Our first patient, S M (Case 215,093) is eight years old. As you see him now he does not seem to be sick at all, he is slightly pale but otherwise quite normal. He was

admitted to the Pediatric Department on November 20, 1921,* with the chief complaint of inability to pass urine for the last few days and swelling of the body for the last six weeks

Family History—This is of no importance

Previous Diseases—He was born at term, labor was normal, was breast fed for one year Three years ago had whooping-cough During the last year has had measles, chickenpox, and pneumonia He has had frequent attacks of tonsillitis and coughs on frequent occasions He had an attack similar to the present one six months ago, which cleared up in eight days There is no history of scarlet fever

Present Illness—This began about six weeks ago with rapid swelling of the whole body, including face and eyes He had been under treatment at home with no effect During the last two days he passed practically no urine, the small quantity obtained being red and turbid He has vomited twice

Physical Examination—The appearance at the time of admission was that of a child of his age, markedly edematous and of a bluish-white pallor Face and eyelids were swollen, as well as the genitals and lower extremities The lungs showed dulness and diminished breathing over both bases The heart was negative The abdomen was protuberant and a fluid wave could be obtained The blood-pressure was 100 systolic and 80 diastolic

The blood count showed 4,960,000 red cells and 88 per cent hemoglobin The white cell count was 18,400, with 74 per cent. polymorphonuclear leukocytes, 21 per cent lymphocytes, and 5 per cent monocytes The urine obtained on the following days showed a large quantity of albumin with numerous granular casts and was of a high specific gravity

The blood chemistry at the start was as follows

Urea nitrogen	19.6	mgm per 100 c c
Total serum protein	4.2	per cent
Cholesterol	0.628	"

* I am presenting this case by courtesy of Dr H Heimann, Chief of the Pediatric Department

The Wassermann test of the blood was negative His basal metabolism was -30 per cent.

As you see, we have here a case which on admission presented all the classical symptoms of chronic nephrosis mentioned above The pallor, the anasarca, the effusion in the serous cavities, the albuminuria with absence of blood in the urine, the typical figures in the blood chemistry, and the absence of hypertension

The boy was treated at home for six weeks without any benefit. While in the hospital, from November 20th until November 30th, the child was on a diet of 500 c c of milk, during which time his condition remained stationary He excreted about 100 to 400 c c of urine daily From November 30th until December 5th he was given 2 grains of theocin three times a day without any effect on the diuresis On December 5th, in addition to the 500 c c of milk, a protein diet consisting of 2 eggs, 15 grams of green peas, and 50 grams of chicken was given From then until December 8th the diuresis increased, and he lost 5 pounds in weight The protein diet was continued On December 12th the blood cholesterol was 0 360 per cent and the serum protein 4 39 per cent On December 15th the basal metabolism was -7 per cent, as you see, a considerable improvement over the first figure

On January 13th (eight days after the inception of the high protein therapy) his blood chemistry was as follows

Urea nitrogen	16 8	mgm per 100 c c
Incoag nitrogen	38 0	" "
Cholesterol	0 242	per cent
Total serum protein	5 68	"

The improvement is obvious You will observe that as soon as the boy was put on a high protein diet the diuresis increased, the edema disappeared, the cholesterol gradually returned to normal, and the protein of the serum increased markedly If we compare his present condition with that which we found on admission and in the interval preceding the administration of the high protein feeding, there can be

no doubt that his improvement is due to the high protein diet

The above case illustrates the effect of high protein feeding only. The next case will show you that sometimes the protein diet alone does not accomplish the same result, and the addition of thyroid therapy is necessary.

A L., fourteen years of age (Case 204,353), she has been subject to frequent attacks of tonsillitis. A tonsillectomy was performed one year ago. Scarlet fever six years ago, so far as can be determined there was no complicating renal factor at the time. For the six months prior to entrance to the hospital there had been gradually increasing edema, dyspnea, frequency, and nocturia. On admission the physical examination was noteworthy only for generalized edema. The urine contained large amounts of albumin, hyaline and granular casts. The blood-pressure was 125/70. The blood chemistry

Urea nitrogen	19.6	mgm.	per 100 c.c.
Inorg. nitrogen	40.3	"	"
Uric acid	2.8	"	"
Creatinin	1.8	"	"
Cholesterol	6904	per cent	

The basal metabolism was -18 per cent.

On admission a diagnosis of chronic diffuse nephritis was made. The patient was put first on the Karell diet, then successively on a carbohydrate and high protein diet, but with apparently little benefit. A salt-free diet and diuretics (diuretin) reduced the edema somewhat, and the weight fell from 106 to 97 pounds, but no further removal of fluid could be effected and the case remained stationary. Then, two months after entrance a high protein diet was again instituted, and, in addition, small doses of thyroid extract were given. Within two weeks the edema had entirely disappeared and the weight had dropped to 85 pounds.

Here we have a case in which the high protein diet had apparently produced no effect until thyroid therapy was instituted. It is quite possible that the failure of the diet at the

beginning, at least, was due to the fact that it was impossible to make the patient eat. The patient still has an albuminuria, although the edema is entirely gone.

Case II—Y. H., forty years of age (Case 207,030). She first entered the hospital on September 25, 1916. The past history is of no importance except that the menopause developed at the age of twenty-eight. For four months prior to admission there had been gradually increasing edema, pain in the lumbar region, weakness, and anorexia.

Physical examination revealed only a marked generalized edema and pallor. The diagnosis on admission was "chronic nephritis." The urine contained heavy traces of albumin, hyaline and granular casts, and a moderate number of white blood-cells. No red blood-cells. The blood chemistry was

Urea nitrogen	21.0	mgm per 100 c c
Incoag nitrogen	56.0	" "
Cholesterol	0.400	per cent

The blood-pressure was 105/80.

For two weeks the patient was on the Karell diet and then on a salt-free diet. There was no subsidence of the edema or increase of the urinary output. On October 11, 1916 she was put on a high protein diet. Within a week there was marked diuresis which continued until the edema had entirely disappeared. This occurred within three weeks of the institution of treatment. She was discharged as a case of "nephrosis" relieved by high protein feeding. The albuminuria persisted.

On January 15, 1921, four and a quarter years later, the patient entered the hospital for the second time. During the preceding year there had been increasing weakness, mental dulness, swelling of the face and lids, and nocturia. On physical examination the patient presented the classical picture of myxedema. The skin was harsh, dry, and scaly, the hair brittle and sparse. The speech was slow and the mentality dull. There was marked swelling of the face and lids, non-pitting edema of the extremities, and the typical subcutaneous infiltrations

of myxedema The urine contained a heavy trace of albumin with many hyaline and granular casts

The blood chemistry was as follows

Urea nitrogen	18.2	mgm	per 100 c c
Incoag nitrogen	37.6	"	"
Uric acid	2.5	"	"
Creatinin	1.9	"	"
Cholesterol	1350	per cent	

The basal metabolism was 20.1 calories, — 19 per cent

In view of the findings the patient was put on thyroid extract. Marked improvement of all symptoms followed. The basal metabolism returned to normal, the blood cholesterol diminished and the loss of 23 pounds in weight in four weeks was noted.

We have here a case which on first admission presented all the classical characteristics of nephrosis, and was markedly improved on a high protein diet. The patient came back four and a quarter years later with all the symptoms of myxedema, and was promptly relieved by the administration of thyroid extract. This patient's present condition, subjectively and objectively, depends entirely on whether or not thyroid extract is given. In this circumstance we find the basic difference between the cases of chronic nephrosis which respond to thyroid therapy and those of true myxedema. In the latter the thyroid therapy must be continued indefinitely, whereas in chronic nephrosis the requirement for thyroid is only temporary in some instances only as long as the edema lasts, in others, until the albuminuria is entirely eliminated.

The cases which I have presented to you here are illustrative of the immediate clinical course which chronic nephrosis ("diabetes albuminuricus") pursues ordinarily and the result which follows under the therapeutic management suggested. Inasmuch as my chief object in the present discussion is to throw more definite light on the nature of the malady in question, I have purposely avoided discussing the different complications that may arise, and which alter the course and therapeutic indications.

Given a case with the conditions as I have described them above, the clinical course is usually uniform and the therapeutic indications are quite clear. The use of the high protein diet with or without thyroid is the only therapy which appears rational under the circumstances.

It should be remembered, as I have illustrated on previous occasions, that cases of chronic nephrosis are curable, not only in the sense that they may be relieved of their symptoms, but in the sense that every vestige of the disease is abolished. The albuminuria must entirely disappear and the composition of the blood should return to normal, and until this occurs the therapy should not be interrupted. To accomplish this six to eighteen months may be necessary.

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CLINIC OF DR JOHN L KANTOR

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ON FIVE COMMON CLINICAL TYPES OF "APPENDICITIS"

THERE is perhaps no abdominal complaint that may at times prove so troublesome to the clinician as pain in the right lower quadrant, or, as it has been aptly termed, "right-side-itis" We owe much, first, to the surgeon (Gibson, Morris, Williams and Slater, Connell) who, by his careful pathologic observations, as well as by the results of his therapeutic efforts, has thrown much-needed light on this subject, and, second, to the roentgenologist (Case, George, and Gerber) who, by visualizing the morphology and the function not only of those organs located in or traversing the right lower quadrant, but of the entire colon as well, has added enormously to our pre-operative and non-operative information in this particular field

There are, to be sure, a number of relatively rare conditions causing pain or tenderness in the right lower quadrant, such, for example, as ileocecal new growth or tuberculosis or intussusception, but these become sooner or later in their course so well defined as to cause no special difficulty in diagnosis, and they will, therefore, not be included in the present discussion It is rather the common, every-day things that here most intrigue the attention, the things that are most commonly called "appendicitis", the things that are perhaps too commonly operated on as "appendicitis", and these things seem, clinically, to fall into five great types or classes

Type I Acute, Subacute, or Recurrent Inflammatory Appendicitis—About this condition there is universal agree-

ment It is classic appendicitis proper and its treatment is unqualifiedly surgical The clinical syndrome is a medical commonplace The patient comes down suddenly with general abdominal cramps, nausea, and vomiting, soon there is fever* and, before long, localization of pain, tenderness, and rigidity to the right lower abdomen The condition is correctly diagnosed by the first doctor to see the case, commonly by the patient himself, and is, as a rule, promptly and properly handled This type needs no further exposition

Type II Pain and Tenderness in the Right Lower Quadrant Without Rigidity or Fever in Asthenic Individuals—This condition is not appendicitis, as such, and surgery is not indicated The subjects of this type are invariably of the asthenic habitus, with slim bodies, long, low-placed viscera, and loose peritoneal attachments Very commonly, indeed, such persons complain of a dull, dragging, or sticking discomfort in the right lower quadrant, and examination reveals tenderness on pressure and at times a palpable and even freely movable cecum In order to interpret such findings correctly it may be helpful at this point to review briefly certain elementary physiologic and embryologic considerations Let us take up first the clinical significance of painful abdominal sensations in general Such sensations may be considered as falling into three distinct (though not necessarily mutually exclusive) divisions †

1 Spontaneous pain due to colic This is purely subjective in its origin, it is intermittent in occurrence, it is, as a rule, relieved by pressure and by the application of heat, and it is caused by increased intravisceral tension anywhere in the hollow organs, as in ordinary intestinal peristalsis, in pylorospasm,

* Comment by Dr A O Whipple, Professor of Surgery, Columbia University "It may be misleading to emphasize the question of fever in acute appendicitis, for we see constant cases of the worst type that have practically no temperature, and in this hospital (Presbyterian) we disregard altogether the question of temperature in the diagnosis Of course, many cases come with acute appendicitis and have a temperature, but it is usually the result of abscess formation, and may not be present at all in the fulminating type"

† Cutaneous hyperesthesia (Herd zones) is too superficial to be confused with the deep-seated pains about to be mentioned

in ureteral and biliary colic Surgery is not essentially indicated

2 Plexus tenderness This is purely objective in origin ("pain on pressure"), it lasts only during the application of such pressure, it is located only at the points of known plexus distribution, and it also is not of primary surgical significance

3 Pain of inflammation This is both subjective and objective in origin, it is constant in duration, it is aggravated by pressure, relieved by cold, and it indicates inflammation, "pathology," pus, etc., and is primarily a surgical phenomenon

To return now to our asthenics In addition to their narrow architecture, such folk are characteristically undernourished, hypersensitive, and "neurotic" Tenderness of the right iliac fossa is in them the rule rather than the exception It is obviously of the plexus type, above mentioned, and is to be explained specifically by ready accessibility and increased irritability of the nerve plexuses at the ileocecal junction (McBurney's point of the surgeon) Such tenderness is on an exact par with that to be found in the epigastrium (solar plexus) and downward along the course of the aorta (sympathetic chain) when the latter is accessible to palpation—so-called dynamic aorta It is highly important to recognize that such tenderness is very common in all emaciated individuals, and that it cannot of itself be accepted as indicative of organic disorder

The second point that may cause confusion is the presence of a palpable cecum This, of course, may be due to some relative obstruction in the distal course of the colon, as will be described under Type III of this presentation In asthenic subjects, however, it is much more likely to be a congenital condition associated with atony (typhlatonia) and increased mobility of the cecum, and it is probably the pull on the mesentery of an overloaded, sluggish bowel that is responsible for the subjective discomfort complained of by the patient This "cecum mobile" (Wilms) has been regarded as an entity, but it is better to look upon it as but a single manifestation of the general tendency to laxness and ptosis characteristic of the asthenic constitution

Of further interest in this connection is the rôle played by defective embryonic development. The congenital viscer-optotic invalid is, as is well known, a veritable storehouse of embryonic misadventures in morphology. In the region of the right lower quadrant such defects are represented by abnormalities in descent and fixation of the cecum in the direction either of deficiency or excess. Thus, we find the freely movable cecum, the low fixed cecum, the more or less peritonealized cecum covered by thinner or denser "veils" or "membranes," and so on. Though believed by Jackson to be the result of chronic inflammatory processes, the preponderance of opinion, surgical (Mayo) as well as anatomic (Harvey), is in favor of the essential embryonic nature of these enveloping tissues. Recent Roentgen studies (Payne and Trahar) also point in the same direction.

Occasionally the membranes just referred to may cause intestinal obstruction of varying degree. In such rare cases surgery is of course indicated, but even here the danger of further "adhesions" is to be kept in mind. In all other individuals of this type surgery should be the very last resort, for it is axiomatic that asthenics, and particularly neurotic asthenics, are notoriously poor subjects for operative interference.

The treatment of so-called appendicitis of Type II, then, is entirely conservative. Measures directed toward relief of the ptosis and atony such as abdominal support, rest, fattening, sedatives, etc. are bound to give results that are satisfactory in proportion to the skill and persistence with which these recommendations are carried out. Fortunately such principles are being gradually acknowledged and the story of "feeling worse after my appendix was removed" is being less and less often heard in consulting room and clinic.

Case I—Persistent pain after appendicectomy, asthenia, achylia gastrica. Trained nurse thirty-one, single. Comes for examination complaining of continual pain around appendix scar. History reveals long-standing invalidism, many acute infections, tonsillitis, endocarditis, nephritis, etc. Twelve years ago vomiting, intense, non-localizing abdominal pain, fever,

diarrhea Six years ago localization of pain to right iliac fossa with persistent diarrhea In general, frequent diarrheas from dietary indiscretions Three years ago appendicectomy for



Fig 200—Illustrating the degree of gastropptosis and atony in Case I This stomach film was made in the standing position The rest of the figures are from films taken in the prone position

"chronic appendicitis with adhesions about head of cecum" Postoperative, only occasional pain until one year ago, when discomfort became constant Always wants to favor the right

side Persistent local soreness Comfortable in the morning, but worse again after several hours' duty

Physical examination reveals extreme asthenic habitus with malnutrition Patient 46 pounds underweight for age and height Tenderness over appendix scar Relief from support of lower abdomen Test-meal shows achylia gastrica (achlorhydria)

Roentgen examination shows marked gastrocoloptosis with atony (see accompanying roentgenogram, Fig 200) No delay in evacuation of stomach Fixation and tenderness in ileocecal region

Comment—The operation in this case was unnecessary The "adhesions" about the cecum were probably congenital Adequate preoperative study should have caused recognition of asthenic habitus and of achylia gastrica The diarrheas and abdominal symptoms were undoubtedly gastrogenous in origin The proper therapeutic indications in this case are, obviously, relief of the ptosis and atony, and administration of hydrochloric acid

Case II—Adhesions following appendicectomy, persistence of symptoms, relief from routine medical management (Note This case was reported last year See The General Management of Functional Digestive Disorders, Med Clin N Amer, 1921 (March), 4, 1550) Railroad brakeman, twenty-eight, married In the spring of 1917 began to suffer from pain in the lower right abdomen, constant, and radiating to the pit of the stomach There were no colics, vomiting, or fever Constipation was severe, the bowels often not moving for a week at a time The condition was diagnosed by his doctor as "intestinal indigestion" Medical treatment for two months brought no relief Operation was performed in June, 1917, for "chronic appendicitis" In four weeks there was return of all previous symptoms Two a-ray examinations were made, and the patient was told that he had "adhesions at the hepatic flexure and gas in the colon" A second operation, performed in June, 1919, revealed a band strangling the small intestine Four weeks after the division of this band there was again

recurrence of the original symptoms This time the patient was advised to have his colon removed However, he hesitated at this proposition and came to us for opinion

Physical examination was negative except for ptosis and malnutrition Abdominal support was ordered, also mineral oil, suprarenal substance, and increased milk consumption The suprarenal substance was soon discontinued When this case was reported (March, 1921) the patient had been having daily bowel movements and had gained 5 pounds in weight Now (one year later) his bowels are still regular, even without the use of the oil He has gained 2 more pounds in weight and his occasional gas distress, which makes him very "nervous," is readily controlled by bromids During practically the entire year he has continued at his original occupation

Case III—Probable congenital low fixation of cecum and of transverse colon Single woman, twenty-two, designer Referred for opinion as to nature of recurrent vomiting History of occasional emesis since childhood upon the least excitement, such as going to the country, being promoted at school, etc., also train sickness up to the age of fifteen Four years ago sudden onset of anorexia, nausea, and vomiting every few hours, the attack lasting ten days Since then repeated attacks, often preceded by sensation of food stopping just before it reached the stomach (cardiospasm²), and continuing with vomiting of food and then bile until the abdomen and sides were sore Many different opinions were obtained from internists, neurologists, a gynecologist, and a surgeon Also many forms of treatment were tried, varying from the usual sedatives and antispasmodics to bed rest, starvation, and rectal feedings All these things were without avail, each attack ran an apparently self-limited course The net result, however, was progressive loss of weight, increasing weakness, and nervousness

Examination revealed a small subject of asthenic habitus, 29 pounds underweight (actual weight 85 pounds) The cecum was palpable and tender, there was relief from support of the lower abdomen Seventy c c of pure green gastric juice were

recovered from the fasting stomach (hypersecretion) Test-meal revealed distinct hyperacidity



Fig 201 —Illustrating condition in Case III Film taken forty-eight hours after barium meal, one stool, reclining position Note low (fixed) cecum despite relative emptying, also low (fixed) midtransverse colon Appendix visible (arrow)

Roentgen examination showed a low, hyperactive stomach of good tonus, emptying within six hours The duodenum was normal The colon filled well but emptied slowly, moderate residues being present at ninety-six hours despite three stools

in that interval. The cecum was found low in the pelvis (Fig 201) at each observation (fixation). The transverse colon was ptosed sharply and its midportion fixed constantly at the level of the bladder. The appendix was continuously visualized, it was filled widely for about an inch. In one observation it looked as if the pelvic colon was fixed to the right at a point near the appendix.

Comment—It is possible, of course, that this case may really belong to Type IV (irritative appendicitis). It is given at this point, however, because it represents a rather common finding, viz., a long-standing history of dyspepsia associated with fixation of appendix and adjacent parts of colon in a young person, nullipara, with negative pelvic history and findings (gynecologist's report) and without any evidence whatever of past appendix inflammation. Under such circumstances it seems fair to assume a congenital malformation as being the responsible factor in the clinical picture.

Type III Right Colon Stasis Due to Spasm or Other Mild Obstructive Condition in the Distal Colon—This condition also is not appendicitis. Whether appendicitis may result from its neglect is an open question. Theoretically such a thing is not impossible, in which case it may be permissible to paraphrase Moynihan's famous dictum that "the cause of most duodenal ulcers lies in the right iliac fossa" to read "the cause of most chronic appendices lies in the distal colon." Be that as it may, the recognition of the nature of this exceedingly common type of disorder is very important, for correct therapy calls not so much for the removal of the appendix as for the relief of the underlying cecal stasis. Clinically, the patients of Type III complain of intermittent or constant abdominal pains along the course of the colon, very commonly in the right lower quadrant, and not infrequently associated with palpable cecal erections. These cecal erections wax in size with the degree of fecal stasis but unfortunately many patients fail to recognize this association. Indeed, it takes careful questioning and at times the employment of special diagnostic methods, such as the x-ray, to bring out a clinical picture that strikingly

resembles, in miniature, that of obstructing distal colon carcinoma, with the difference that in the case under discussion we are dealing with long-standing, benign factors such as spastic constipation, redundancy of the pelvic colon, some forms of colitis (both mucous and inflammatory), and anorectal conditions, such as dyschezia and spasm, whether idiopathic or secondary to local disease (fissure, ulcer, piles). Any such obstruction to the fecal column, particularly when its action is intermittent or recurrent, tends to throw back the contents to the head of the colon (exaggerated antiperistalsis), and thus brings on the usual sequence of hypertrophy and dilatation, with local irritation and subjective discomfort.

In taking the history of such individuals one should not be misled by the patient's bare statement that the bowels move daily or even several times daily. Often, specific inquiry as to the size, bulk, formation, and consistency of the stools is necessary to unmask a true, spastic constipation. It is well to bear in mind that the normal adult stool is composed of one or more homogeneous, soft, sausage-like segments, each at least the thickness of a thumb, and representing in length a total of 10 to 12 inches, which is approximately the extent of the lower gut (pelvic colon and rectum) ordinarily evacuated in the normal act of defecation. Any undue thinness of the excrement (pencil stool) or increased hardness or fragmentation (marble or sheep dung stool) is strongly suggestive of a spastic condition in the lower colon, rectum, or anus. Likewise, one should not overlook the essentially similar nature of what look like normal segments, but what are really conglomerate masses composed of small marbles originating in a spastic descending colon and packed together in the ampulla of the rectum*. Finally, suspicion should attach to a history of repeated small, formed stools—to be distinguished from frequent loose evacuations, *i. e.*, diarrhea—for such defecation in instalments is also suggestive of spasticity.

* For an interesting theory expressing an opposite viewpoint see Burnett, who holds that such "mosaics" consist of fecal units and are indicative of a "normal intestinal rate."

Roentgen studies are of particular value in these conditions. Although it is impossible to go into technical details, it should nevertheless be pointed out as eminently desirable that the entire digestive tract be investigated, utilizing mouth filling and opaque enema, and that the whole procedure be controlled by fluoroscopic as well as radiographic methods of observation. Mouth filling gives the bulk of the evidence as to spasticity, colitis, and constipation in general. In spastic states there is a very characteristic retention of the barium in the cecum and ascending colon which seem to be distended and tightly packed. The distal colon, on the other hand, is narrow and shows deep-cutting haustrations or small individual segments exactly comparable to the pellets of the sheep dung stools. The slow feeding of the meal from the right-sided reservoir through the parts of the colon involved in the spasm can be strikingly followed from day to day by means of the barium meal by mouth. The very frequent filling of the appendix in these cases may possibly be due to the increased back-fire into the proximal part of the large intestine.

For the diagnosis of redundancy of the large bowel simultaneous filling of the entire colon is desirable. This is adequately obtained by the use of the opaque enema as ordinarily practised.

The principles of treatment of the various conditions making up Type III are now pretty well understood and therefore do not need special description in this paper. A few remarks in regard to the management of spastic conditions may perhaps be pardoned. In addition to the usual forms of therapy—rest, mental and physical, bland diet, general sedatives (drugs, warm baths), specific antispasmodics (atropin), oil injections, colon irrigations, avoidance of violent purges, etc.—there are two newer methods of treatment that give promise of usefulness. The first is repeated transduodenal flushes with hot hypertonic salines according to the method of Jutte. The other is a procedure devised by Soper and based on Meltzer's observation that solutions of magnesium sulfate, when applied to the intestinal mucosa, tend to overcome intestinal spasm. The technic is as follows. An ordinary sigmoidoscope is intro-

duced to the point of spasm, and direct applications are made "to the contracted area by means of cotton applicators soaked in a saturated solution of magnesium sulfate. When the contractures are above the reach of the sigmoidoscopic tube a soft catheter is introduced through the instrument and 1 to 2 ounces of the solution are injected. In moderate contractures six to eight treatments usually suffice to overcome the spasticity and permit the restoration of normal colonic function. Severe cases may require a larger number of treatments spaced over a period of two to three months' time. The same treatment is efficacious in spastic contractures of the rectum. It must be noted, however, that the magnesium sulfate solution has no effect whatsoever upon sphincter spasm of the anal canal. The indications for treatment of sphincter spasm are direct instrumental dilatations and appropriate treatment of the accompanying lesions of the mucosa."

The writer has used this method with satisfaction. As a rule each treatment seems to be followed by an increase in the size and bulk of the stools and by greater freedom of evacuation. A wider use of this method is to be recommended.

Case IV—Palpable tender cecum diagnosed tuberculosis or chronic appendicitis, spastic colon, anal sphincter spasm due to hemorrhoids and proctitis. Lawyer, twenty-six, married, came under observation October 23, 1921, complaining of a "lump" in the right lower quadrant, weakness, and recent diarrhea. In the past the bowels had always moved daily, but the patient never could take an enema because he had trouble both in introducing the tip and in expelling the fluid. Three years ago he experienced a sudden attack of general abdominal discomfort at night partly relieved by enema. No localization of pain at that time. About two years ago he had "influenza" with much gas distress and constipation. Four months ago there was an attack of pleurisy and discovery of a healed apical tuberculous lesion. Two months ago an attack of diarrhea lasting one week with much tenesmus and gas distress. At this time the patient palpated his own cecum, describing it as a lump the size of a watch in the lower right side. There

was no tenderness, but there was a dull, heavy feeling when lying on the back or on the left side. The lump seemed to disappear when lying on the right side. There was considerable



Fig 202 —Illustrating colon condition in Case IV. Film taken at twenty-four hours post cibum, one stool. Note high degree of spasticity throughout. White arrow points to appendix; black arrow, to rectal spasm.

variation in size at different times. The patient then consulted a surgeon, who diagnosed either tuberculosis of the cecum or chronic appendicitis.

Physical examination, October 24, 1921, showed a small, asthenic subject, 28 pounds underweight. Pulse and temperature normal. Cecum palpable and tender. No rigidity. Marked relief from support of lower abdomen. Proctoscopy painful. Numerous external hemorrhoids. Tight and inflamed sphincter. *Test-meal negative.*

Roentgen examination. Stomach and duodenum normal except for hyperperistalsis. No ileal stasis (at nine and a half hours). Colon still faintly outlined at seventy-two hours, despite three stools. The entire colon very spastic (Fig 202), especially from hepatic flexure onward. Distinct rectal spasm observed (in addition to anal spasm noted on physical examination). Appendix filled near the tip at twenty-four and forty-eight hours. The cecum was free and showed no filling defects or increased irritability either by mouth meal or by colon injection. It was tender throughout the examination.

The stool was negative for tubercle bacilli.

Course. Local treatment for rectal condition. Fattening diet, including olive oil, abdominal binder, sedative mixture, one or two magnesium sulfate instillations. At the present writing, more than three months after the first visit, despite the fact that treatment was not very thorough, the patient has practically no distress in the right side, the "lump" has almost completely disappeared, the bowels are moving freely and regularly, and there has been some gain in weight and strength.

Case V—Tender, gurgling cecum, redundant colon. Married woman, twenty-two, came under observation July, 1920, complaining of pains across lower abdomen and of constipation. The constipation dates back to childhood. The average stool interval was three to four days, but sometimes the bowels were not opened for a week. Evacuation was had only by enema. Cathartics generally caused cramps and no stool. There seemed to be no distress from the constipation as such. In 1916 two attacks of epigastric cramps, not relieved by enemas. In 1918 the patient began the use of mineral oil, with the result that she had a formed stool each day. Had dyspepsia of pregnancy (heart-burn) the next year. Since

childbirth, June 1920, she has had to use daily enemas. At the end of June she had a severe attack of epigastric pain lasting four or five days. One week ago took an enema, but the



Fig. 203—Illustrating Case V. Film taken twenty-four hours after mouth filling. Note excessive distances from cecum to hepatic flexure and from midtransverse colon to splenic flexure. A case of elongation of the proximal, and redundancy of the distal, colon.

water did not return. The excessive straining during this experience brought on pains in the epigastrium and down the thighs. These sensations are worse when standing and bear

no relation to meals. Soreness on pressure in lower abdomen. Sense of incomplete evacuation after enemas.

Examination showed a well-built and well-nourished young woman. The abdomen was soft, there was moderate tender-



Fig. 204.—Same case as Fig. 203. Film made after administration of opaque enema. Note great redundancy and looping of distal colon.

ness below, more in the right iliac fossa than in the left. The cecum was gurgling. The Meltzer sign was moderately positive. The test-meal showed a hyperacidity.

Röntgen examination (Figs. 203, 204) revealed a striking

state of affairs in the colon which was enormously increased in length and redundant. From the cecum, low-placed in the pelvis, to the hepatic flexure was 1 foot in height, from the lowermost point of the transverse colon to the top of the splenic flexure was 2 feet in height. The colon distal to the splenic flexure was involved in six distinct loops or convolutions, and if the chief flexures are added, this particular patient could boast of eight loops in her large intestine. The splenic loop stored an enormous amount of gas ("aerocolie" of French authors). The progress of the barium meal given by mouth was observed for seventy-two hours, and then, no spontaneous bowel movement having taken place, the colon was emptied by cathartics and enema in order to proceed with the barium injection per rectum.

Comment—It is easy to see how this case might have been misdiagnosed and the appendix removed without alleviating either the pains or the underlying constipation. The diagnosis of redundant colon by physical examination is well-nigh impossible. Examination of the rectum reveals no fecal accumulation, for the delay is invariably above the pelvic rectal flexure. The value of Roentgen study in such cases, is, therefore, self-evident.

Case VI—Subacute appendicitis syndrome, dyschezia. High school girl, seventeen, complaining of epigastric pain, vomiting and constipation. Four years ago onset of constipation due to neglect of bowels. Maximum stool interval four days. Occasional bleeding from piles. Three months ago there was gradual onset of pain in the epigastrium at variable intervals after meals, and occasionally at night. There was vomiting of large quantities of food and much gas distress. Increased use of cathartics. The present attack began five days ago with fever (102° F), malaise, headache, complete anorexia, severe epigastric pain, vomiting, and belching. Examination revealed tenderness in the epigastrium and in the right iliac fossa.

Roentgen examination (Figs 205-207) showed a six-hour residue in the stomach and, at every observation, an incompletely filled, spastic, duodenal cap. The colon was still heavily

filled at one hundred and twenty hours, despite two small stools during this interval. There was spasticity of the distal large intestine. The ampulla of the rectum was packed with feces.

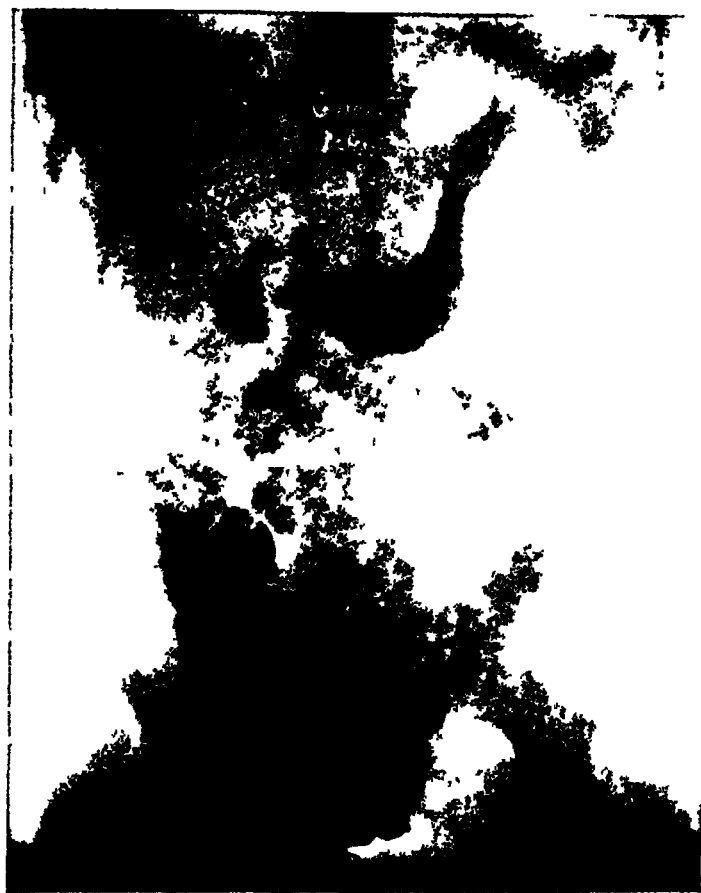


Fig. 205—Illustrating Case VI. Film taken six hours post cibum. Note residue in stomach, also incomplete duodenal cap. The transient gastric retention and duodenal spasticity in this case are reflex phenomena due to dyschezia.

without producing the desire to defecate (classic dyschezia). The cecum was tender, but not fixed, as proved by its gradual elevation on emptying. The appendix was persistently filled.

Course Enemas and irrigations were ordered, to be followed by a dose of "Laxol" There was a complete disappearance of symptoms



Fig 206—Same case as Fig 205 Film taken seventy-two hours post cecum, one stool Note higher position of cecum than in Fig 205 (no fixation), also appendix filling (arrow) and beginning accumulation in ampulla of rectum

Comment—Despite the short period of observation, and the absence of a re-examination, it seems fair to assume that the

entire clinical picture might be the result of a reflex from the rectal stasis, particularly as such secondary phenomena as



Fig. 207—Same case as Fig. 206. Film taken one hundred and twenty hours post cibum: two small stools in all. Note still further elevation of cecum and appendix (arrow) also marked spasticity of pelvic colon and large mass in ampulla without provoking the desire to defecate (*dychezia*).

duodenal irritation and pyloro-spasm are by no means uncommon in children suffering from coprostasis.

Type IV Low-placed, Fixed, and Tender Cecum Secondary to Disease of Some Other Organ in the Right Iliac Fossa.—In this type the fixation is not congenital as in Type I but is inflammatory in nature and acquired in origin. It is the result of a primary process in some adjacent structure such as the



Fig 208 —Illustrating Case VII. Note low position of heavily loaded cecum at six hours post cibum and compare with similar position at forty-eight hours (see Fig 209)

uterus and adnexa, pelvic colon, peritoneum, etc. Before the advent of the x-ray the condition was generally not discovered prior to laparotomy for the underlying cause. At present, on the other hand, very precise preoperative information is available from Roentgen study.

Case VII—Low cecum adherent to cystic ovary. Married

woman, twenty-eight, referred by gynecologist to clear up condition in right lower quadrant. For past week the patient has suffered from colicky epigastric distress, also from twitchings in the right iliac fossa, worse on moving about and on pressure.



Fig. 209—Same case as Fig. 208. Note low position of partially emptied cecum at forty-eight hours. Failure to rise when empty means fixation. Compare with Fig. 208. Cecum is probably adherent to cystic right ovary.

No vomiting. Pains are relieved by lying down with hot-water bag. Previous history of diarrhea, but no typical appendix attacks. Long-standing dysmenorrhea. Pelvic examination reveals large cystic right ovary.

Röntgen examination showed normal stomach and duode-

num The large bowel filled rapidly, but emptied rather slowly, there were slight residues at seventy-two hours despite daily bowel movements. At every observation the cecum was found low in the midpelvis (Figs 208, 209) and seemed fixed at that point to the adnexa, the pelvic colon, or to both structures. This position was constant, no matter what the degree of filling. The cecum was moderately tender. The appendix was not visualized.

Secondary fixation of the cecum was diagnosed in this case.

Case VIII—Low cecum, possibly adherent to tuberculous fallopian tube. Girl, twenty-one, tuberculous, complains of recurrent pains in right lower abdomen, nausea, and vomiting. Two years ago onset of nausea after meals. Nineteen months ago acute tuberculous pneumonia. At the same time an attack of pain in right iliac fossa, treated by "freezing." Since then persistent nausea and anorexia. Four months ago recurrent attack of pain in right lower abdomen, sticking in character. For past five to six weeks almost complete anorexia, nausea, and vomiting of bile in the morning. Vomiting worse during menses, but periods are regular and apparently normal except for severe pain (dysmenorrhea).

Physical examination shows well-nourished girl. Classic lung signs at left upper lobe. Temperature 100.3° F by mouth, pulse 84. Abdomen shows tender, gurgling cecum. Relief from support of lower abdomen. Test-meal shows low free and high total acid.

Roentgen examination. Preliminary fluoroscopy of chest shows "infiltration" of left lung. Stomach and duodenum normal except for moderate gastric atony. Colon practically empty (except for slight cecal residue) at forty-eight hours, after two stools. At every observation the caput coli was fixed low in the pelvis (Fig 210) in the neighborhood of the right adnexa and the pelvirectal colon. There was constant tenderness of the ascending colon at a point where the retrocecal appendix was subsequently revealed.

Comment—A tentative diagnosis of primary tubal tuberculosis may very properly be made in this case. The differential

diagnosis lies, of course, between that and a recurrent inflammatory appendicitis. Operative findings are not available at the present writing.



Fig. 210—Illustrating Case VIII. Note low position of cecum at nine hours post cibum. Retrocecal appendix visualized at subsequent examination. Condition probably due to tuberculosis of right adnexa.

Type V Chronic Irritative Appendicitis—This is perhaps the most interesting of all the forms of appendicitis. Although the treatment is invariably surgical, the diagnosis may unfor-

tunately be so difficult to make that the proper curative procedure may be unduly postponed or even entirely neglected. Generally speaking, the symptoms may be those of anything but "appendicitis." The usual clinical picture is predominately that of gastric irritation and shows the familiar "hyper" syndrome—hyperacidity, hyperperistalsis, hypermotility. Often there is hunger-pain, vomiting, and tenderness in the epigastrium, and when this is associated with defective filling of the duodenal cap, with or without gastric retention, the diagnosis of duodenal (or gastric) ulcer is inevitably made. The chief distinctive feature is that the usual treatment for ulcer (rest, frequent small meals, sedatives, alkalies) gives no, or at the most only transient, relief. If careful and repeated examination is made of the right iliac fossa, suggestive tenderness and moderate rigidity may be evoked sooner or later. Perhaps more commonly pressure in that region may cause referred pain at the umbilicus or in the epigastrium (where the usual subjective distress is experienced). A long period of observation may be necessary to arrive at the proper diagnosis. In some cases an exploratory laparotomy is the only hope left to the patient. Under such circumstances it is quite proper to remove the appendix as a therapeutic test provided no more likely causative factor has been revealed by the operation. Strangely enough, the offending appendix may appear quite normal in every particular. The surgical results obtained in this type of appendicitis are generally most satisfactory, as shown in the following illustrative cases.

Case IX—Ulcer syndrome, appendicectomy, complete recovery. Single man, twenty-two had suffered from epigastric pains for three years. Was treated for ulcer without improvement. Roentgen examination, February, 1920, showed gastropsis and atony with hyperperistalsis, but no delay in emptying. The duodenal cap was persistently defective. The colon was practically empty in forty-eight hours. The appendix was filled and tender at each observation. A diagnosis was made of reflex duodenal irritation with intermittent pylorospasm possibly due to appendicitis.

In March, 1920 the patient was operated on and an "acute exacerbation of a chronic appendicitis" was found



Fig 211 —Case of possible chronic irritative appendicitis (not described in text) Note atypical position and wide continuous filling of appendix Film at twenty four hours post cibus

He has just reported (two years after the first observation) that he gained 20 pounds after his operation and feels "fit as a fiddle"

Case X—(Contributed by Dr Marks S Shaine, Assistant



Fig 212—Case of probable irritative appendicitis (not described in text) History of typical hunger-pains for twenty years No relief from ulcer therapy Examination shows sthenic habitus and tenderness in left epigastrium No pain or tenderness in right iliac fossa Note long, curved (non tender) appendix, with tip fixed retrocecal Film taken at twenty-four hours post cibum The duodenal cap was constantly "spastic" There was no gastric retention

in Gastro-enterology, Vanderbilt Clinic) Persistent dyspepsia for six years, failure of all medical treatment, immediate and

permanent relief after appendicectomy. Married woman, twenty-nine, came under observation in January, 1921. Past history negative. Six years ago onset of vomiting, belching, and general abdominal pain bearing no relation to meals. After nine months the vomiting and belching stopped, the pain continued. Four months ago (October, 1920) the vomiting and belching recurred. The vomiting comes on one hour after meals, the ejecta taste sour, this is never blood. No vomiting takes place before meals, on arising, or late at night. The belching takes place one to two hours after meals. There are frequent severe headaches. The bowels are regular, the appetite is fair. The cramps often cause palpitation and dizziness, and the patient has fainted on two occasions. The pains are never severe enough, however to double the patient up. The pain is more on the right side, is drawing in character, and radiates to the back. There are no urinary symptoms. There is no nervousness. The patient has lost about 8 pounds in weight.

Examination, January, 1921. Abdomen tender in epigastrium and below umbilicus in midline. No appendix tenderness. No organs felt. Free acid 17, total 40.

Therapy. Bromids, valerian, hyoscyamin, bismuth cerium ovalate, atropin, anesthesin were employed without the slightest relief. Lavages were tried every third day with similar results. Electricity was applied intragastrically in the form of galvanism, with relief for just one day. Even cocain and morphin made no impression. The patient was then admitted to a hospital, where an x-ray examination proved negative and the test-meal confirmed the previous findings. Lenhartz diet was instituted, but the vomiting and pain persisted. A neurologist diagnosed "neurasthenia" and suggested that the patient be fed but one meal a day, which she vomited none the less. After three weeks of hospitalization the patient became so prostrated that whereas she had walked into the institution she had to be removed on a stretcher. Duodenal feeding was next attempted, but the tube was not retained. Almost in desperation, the patient submitted to exploratory operation May, 1921. The stomach, gall-bladder and appendix appeared normal. The latter was

removed. The patient vomited just once after operation and never thereafter. Today, eight months later, she has gained 19 pounds and is absolutely free from symptoms.

One final point demands consideration. How long dare one wait with operation in doubtful cases? Appendicitis is, after all, a tricky disease, and is it not better to risk the chance of several unnecessary operations rather than to let even one case go on to possible appendix rupture, peritonitis, and death? Anyone who has seen this happen must needs be impressed by the element of uncertainty connected with this disease. The present article has been written largely with the purpose of bringing this very problem to the foreground. The value of individualizing (and "typing") cases has been suggested as a step forward in the solution of this question, but no test has as yet been generally accepted as differentiating sharply between surgical appendicitis and the various conditions that may mimic it. The nearest approach to such a universally applicable criterion is Dr. Bryant's observation that "the asthenic individual may have a chronic appendix for years, but the chances are ten to one that it will never kill him, whereas, if the asthenic subject ever gets appendicitis, it is likely to be primary, fulminating, and apt to flood the peritoneum with pus, and to cause sudden death." This, according to the same author, is the natural result of rather constant anatomic differences in the shape of the appendix: in the asthenic the base of the organ is wider than the top, in the sthenic the reverse is the case, so that in the latter the appendix acts as a closed tube for the cultivation of bacteria. Furthermore, in an extensive autopsy experience Bryant found that "it was without exception the perfectly developed, beautifully modeled, sthenic type of child which died of fulminating appendicitis, the scrawny children died of other things, but not of primary trouble in the appendix."

It would be in the highest degree desirable for surgeons of wide experience to check up their cases and present definite data based on observations of habitus from which universally acceptable conclusions as to the usefulness of this criterion

might be arrived at. That it is quite in keeping with the teaching that asthenics tend to functional, whereas sthenics tend to organic, digestive diseases, is obvious. In the writer's hands this test has proved of value though it is realized that a limited non-surgical experience may be misleading. There seems to be increasing agreement as to the correctness of the statement (see under Type II) that operation can, generally speaking, be safely deferred in the presence of pain and tenderness in the right iliac fossa when this occurs without fever or rigidity in *asthenic* subjects. The converse may quite possibly be equally true, viz., that the same syndrome in *sthenic* individuals should be regarded as potentially surgical unless proved otherwise. A rational conservatism demands that only the most watchful waiting be practised, and that no such patient should be dismissed from observation unless appropriate investigation (such as that partially outlined under Type III) reveals some definite distal colon condition to account for the "appendix syndrome," and, furthermore, unless this syndrome is promptly relieved by appropriate medical treatment. The following case is sufficiently impressive to warrant citation in support of this proposition.

Case XI—Single man, twenty-eight, taxi overseer, came under observation July 26, 1921, complaining of recent abdominal cramps. The history revealed irregular eating habits for fifteen years, and for five years heart-burn and nervousness. One year ago onset of indefinite abdominal distress with occasional constipation. For the past two months increasing general abdominal cramps fifteen minutes after meals, lasting one-half hour, also increasing "nervousness." For the past three days sticking pains and dragging sensation in the right lower quadrant.

Examination revealed a stocky subject, soft abdomen, no tenderness. The stomach test showed a low free and a normal total acidity with increased mucus. The Roentgen examination indicated gastric hypertonus and hyperperistalsis with normal emptying. The duodenum was negative. The proximal transverse colon was looped and seemed adherent to the ascending. The appendix was not visualized. The temperature was not

taken, but on three different occasions the pulse-rate was 74, 74, and 62

The patient was put on sedative and antispasmodic treatment and permitted to go to the country under promise to return at once on aggravation of the symptoms. One month later he was no better, and examination revealed some tenderness in the right iliac fossa. In view of the difficulty of restricting and carefully observing a patient of his temperament, and with regard to his habitus, operation was advised, but it was refused. The man then disappeared from observation.

Three months later, as learned by subsequent report, the patient was dead. He had finally submitted to surgery. A pus appendix was found and removed, but a peritonitis developed which proved fatal in three days.

CONCLUSIONS

1 Pain and tenderness in the right iliac fossa do not always spell true appendicitis

2 Chronic irritative appendicitis may exist without pain and tenderness

3 Conditions under which a diagnosis of "appendicitis" might naturally be made fall into five distinct classes or types as follows

Type I Acute, subacute, or recurrent inflammatory appendicitis

Type II Pain and tenderness in the right lower quadrant without rigidity or fever in asthenic individuals

Type III Right colon stasis due to spasm or other mild obstructive condition in the distal colon

Type IV Low-placed, fixed, and tender cecum secondary to disease of some other organ in the right iliac fossa

Type V Chronic irritative appendicitis

4 There is at present no universally accepted test according to which cases demanding surgical intervention may readily be discovered when the clinical findings are atypical. Consideration of the body habitus may serve as such a criterion

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CLINIC OF DR JESSE G M BULLOWA

FROM THE MEDICAL SERVICE OF HARLEM HOSPITAL,
DR L K NEFF DIRECTOR

A CASE OF HYPERNEPHROMA WITH SPINAL METASTASES

THIS patient, a laborer sixty-one years old, first came under observation in another hospital with the following story until two months before admission he was well, when while handling coal he felt a sudden pain in the right groin and in the right side, radiating to the back, two weeks subsequently he discovered a swelling in the right groin. He has not worked since. His bowels are constipated and there is nycturia two or three times each night since the onset of the hernia.

The physical examination states that the patient was fairly well developed and poorly nourished. The lungs showed no râles, resonance and breathing were normal. There was a systolic murmur at the apex and base of the heart. The abdomen revealed no masses, rigidity, or tenderness. There was slight fullness in the right groin but no true hernia.

Under local anesthesia, on July 9, 1921, he was operated for right indirect inguinal hernia. An empty sac was found. On July 22d it is recorded that he still complained of pain in the right side, radiating to the back. This was attributed to the hernia at a University Medical Clinic and also at the hospital. The pain persists after the operation and has no relation to meals, there is no nausea and vomiting. There has been no dysuria or blood in the urine. There is occasional slight rigidity of the right side of the abdomen. On July 25th he was discharged, with the following significant note: "Operation for right inguinal hernia. Recovery good. Has complained of

pain in the back, not judged to be a surgical condition, probably lumbago "

On November 2, 1921, this patient was admitted to the medical service of Harlem Hospital. A family history obtained then by the house staff is as follows. Father died of cystitis developing into kidney trouble, mother died of cancer of the stomach. In the previous history it is recorded that until a year ago the patient was a heavy drinker of alcohol. In childhood he had scarlet fever and measles. Twenty years ago he had pneumonia. Three months ago he had a herniotomy. There is no history of venereal disease. The pigmented mole on the left side of his face has been present since childhood.

The present illness is of three months' duration and is attributed to overlifting. His chief complaints are stomach trouble, pain in the lumbar region and in the back, and also a small lump in the back. His stomach trouble has become gradually worse, and consists of a gnawing or sticking pain in the epigastrium that starts usually about half an hour after a meal and radiates to both upper quadrants. Pain lasts up to, and is relieved by, the next meal. There has never been any vomiting. No black stools have been noticed by the patient. He says a bowel movement sometimes relieves the pain. Pain in the small of the back has been noticed for some time. The pain is a dull ache across the lumbar region, worse on standing up than on sitting down. Occasional pain down the legs accompanies the lumbar pain. The mass in the lumbar region of the spine was never noticed until three weeks ago. The mass gives the patient no pain or any other trouble, though he seems inclined to attribute to it his lumbar pain.

Physical Examination—The patient is an old white man who appears ill.

Pupils react to light and in accommodation, they are equal.

Ears. No discharge or topus.

Nose. No discharge. Mucous membranes are dark red.

Tongue is moist.

Teeth. Many are missing, others show caries and gingivitis.

Throat. No congestion of membranes.

Cardiovascular Apex is in the fifth space, just outside the nipple line. The sounds are of fair quality. There is a systolic murmur at the apex and at the aortic area, where it is loudest. It is transmitted into the vessels of the neck. The radial pulses are equal, regular, and full.

Lungs Normal resonance, breath and voice throughout.

Abdomen Soft, no masses, tenderness, or rigidity excepting very slight in the left upper quadrant.

Liver, kidney, and spleen are not palpable.



Fig 213—Patient in recumbent position, showing tumor mass, with large veins

There is the scar of a right herniorrhaphy.

Genitals are normal. The prostate is not enlarged.

Skin Normal except for the small pigmented mole on left side of the nose.

Lymph-nodes None palpable except in right inguinal region.

Bones and joints Normal.

Sensation and reflexes Normal except for a zone of hyperalgesia corresponding with the left ninth dorsal segment.

To the left of the midline of the back (Fig 213) at the level of the twelfth dorsal vertebra is a mass about 8 cm square, elevated from the skin 1½ cm, about as dense as contracted muscle. The skin moves freely over it. It is adherent to the deeper parts, from which it seems to arise. There is no constriction at the base. There are large veins about the upper portion. There is an expansile pulsation synchronous with the heart-beat, and a loud bruit, especially marked over the upper portion. There is slight tenderness on firm pressure over the lumbosacral and sacro-iliac joints. There is no tenderness on jarring the spine when the patient comes down on his heels. There is some pain on extending the spine, none on flexing it.

Temperature is 100° F. Pulse is 86. The respirations are 22. Blood-pressure is 125/80 on both sides.

Urine: Amber, clear, without macroscopic blood, specific gravity 1020, reaction acid, a trace of albumin, no glucose, a few hyaline casts and a few red blood-cells were present.

White blood count 9200. Polymorphonuclears 72 per cent; transitionals 3 per cent, lymphocytes 25 per cent.

Blood Wassermann was negative on two occasions.

Stools showed no macroscopic or microscopic blood.

On November 17th a lumbar puncture was made. The fluid was clear, without increased pressure. There was no change in the size of the tumor after puncture or change in the pulsation. The Wassermann, the colloidal gold test, the cell count, and the chemistry of this fluid were normal.

The tumor was aspirated on two occasions with fine needles. After passing through a dense membrane, bright red blood was aspirated. This was sent to the laboratory for examination, and when sectioned no tissue other than blood was demonstrated.

An x-ray examination of the spine (Figs 214, 215) shows a rarification of the bodies of the ninth and tenth dorsal vertebra with a projection forward of the anterior wall and a condensation of the margins. The spinous process of the eleventh vertebra is not visualized. The tumor mass is indicated. Compare this with postmortem section of spine (Fig 216).

When the patient was admitted he was able to be up and about. About four weeks later he complained of numbness in



Fig. 214—x-Ray of the spine (lateral). Note rarification of bodies of ninth, tenth and eleventh dorsal vertebræ with protrusion of the anterior margin and condensation at the edges of rarifications. Note also absence of spinous and transverse processes of twelfth dorsal vertebræ, and rarification of eleventh. Note normal intervertebral articular surfaces and cartilages.

his legs and he was unable to move them freely. The next day there was retention of urine and after that he had to be cath-

terized The pain in his back and extremities became so extreme that he was narcotized with morphin constantly A typical



Fig 215—x Ray of the spine (oblique) Note rarification of bodies of ninth, tenth, and eleventh dorsal vertebrae with protrusion of the anterior margin and condensation at the edges of rarifications Note also absence of spinous and transverse processes of twelfth dorsal vertebra, and rarification of eleventh Note normal intervertebral articular surfaces and cartilages

transverse myelitis developed with loss of sensation below the umbilicus and increased for a segment above that The deep

reflexes were exaggerated, there was involuntary defecation and unnoticed overflow micturition, which required catheterization. The temperature, which had been 100° F, rose to 101.5° F, and the pulse, which had been between 80 and 90, rose to above 100. A cough developed, with extreme prostration, and death

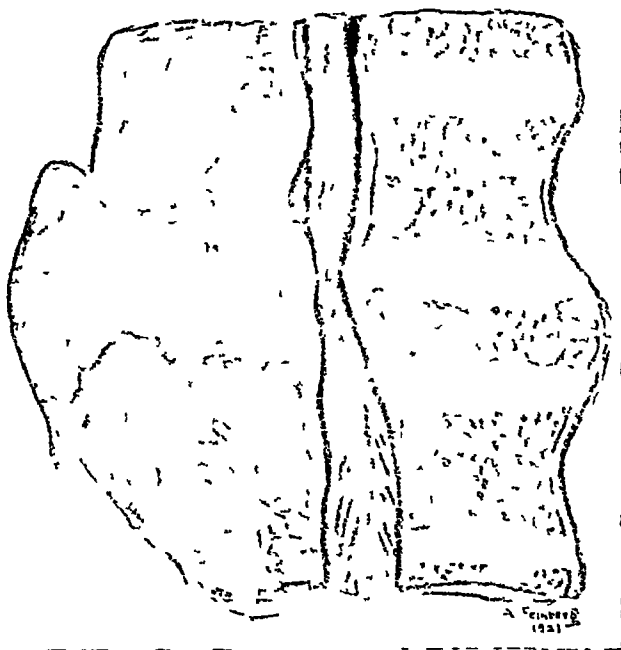


Fig. 216.—Drawing of postmortem section of the spine and spinal cord. It reveals involvement of the spinous processes of the ninth, tenth, and eleventh dorsal vertebrae with protrusion of the tumor behind. The muscles are invaded and displaced by the growth. Note the intact intervertebral cartilages and compression of spinal cord. Note also the lobulated character of the margin and body of the growth and the capsule.

occurred on December 5th. The patient had been narcotized with morphin and there was no increase in the frequency of respiration.

During the first two weeks in bed the patient made no complaint of pain and was apparently comfortable. After that he

required morphin to procure sleep, although his days were good. An attempt was made to secure fixation of the spine with a plaster-of-Paris jacket. This was unsuccessful, even though a window had been cut for the pulsating tumor. The jacket afforded some support, but did not immobilize the spine sufficiently to abolish pain, and was discarded for a time.

The diagnosis presented considerable difficulty. The outstanding feature of the case was the pulsating tumor. This had to be explained. It could have been either an aneurysm, a cystic tumor to which pulsation was transmitted, or a primary or metastatic pulsating tumor. The systolic murmur at the base of the heart, transmitted to the vessels of the neck, pointed to an aortitis, and suggested a *dissecting aneurysm* of the thoracic or abdominal aorta. In favor of this diagnosis was the man's age, the history of sudden onset after a strain, the pulsating tumor from which arterial blood was aspirated, the apparent erosion of the bodies of the vertebrae without involvement of the cartilages, the presence of blood in the urine, and the onset of paraplegia. The fact that the paraplegia came late, after the pulsating tumor had appeared in the back, was against this interpretation, as it is difficult to understand how the cord and nerves could be spared. The involvement of several vertebrae without uniform distribution of the necrosis was also against this view.

The possible cystic masses which were considered were first an *empyema necessitatis*, or pulsating empyema. Against this was the history of acute onset of pain after a strain without history of pulmonary infection, and the absence of physical signs in the lung, as well as the location of the tumor. Another possible cystic mass was a *cold abscess* of Pott's disease of the spine, with pulsations transmitted from the cerebrospinal canal. Against this was the x-ray picture, which showed no involvement of a joint surface such as is characteristic of tuberculous invasion of the bone, the absence of jar tenderness, and the aspiration of bright red blood from the tumor. Another cystic mass considered was a *spina bifida occulta*. Such tumors communicate with the spinal canal and the lumbar puncture

would have caused a diminution in the size of the tumor. The absence of any disappearance of sensation or reflexes was also against this diagnosis. The presence of blood on aspiration was also against it.

A primary *endothelioma* or *perithelioma* had to be considered. An *angioepithelioma* arising from the bone or dura mater was a possible diagnosis. The multiple involvement of vertebrae with areas of good bone was against this view. Moreover, this would have left unexplained the presence of microscopic blood in the urine. In Marckwald's tumors the long bones are involved.

A similar x-ray picture might have arisen from a *metastatic growth* arising from the *stomach* or the *prostate*, but such a tumor does not exist with absence of blood in the stools, and the absence of evidence in the prostate. The stomach-tube was not passed because the presence of a dissecting aneurysm could not be excluded. The remarkable method of visualizing the kidney by injection of gas into the perirenal fat so ably developed by Carelli was not yet in vogue. If this method had been employed it is probable that the correct diagnosis could have been made with great assurance, for the primary tumor in the left kidney would have been visualized. The diagnosis of *hypernephroma*, or Grawitz's tumor, was made because of the fact that we had a pulsating metastatic tumor which had apparently originated from bone with the primary origin in the kidney as suggested by the presence of red blood-cells in the urine, and the fact that on admission there was hyperalgesia and rigidity which might have been referred to distending pressure in one renal capsule. Hypernephromas metastasize frequently into the membrane or flat bones. There were no facts which could be marshalled against the diagnosis of hypernephroma, and the autopsy proved it to be correct.

In brief, the autopsy revealed atherosclerosis of the aorta. There were no stellate scars such as occur in syphilis. The lungs showed a general patchy bronchopneumonia. Examination of the left kidney revealed a tumor in the upper half, protruding on the posterior surface of the kidney about the size

of a tennis ball, encapsulated, tawny yellow, with areas of necrosis. It was a typical hypernephroma. There was apparently no extension into the veins. The condition of the spine and spinal cord is best understood by referring to the illustration (Fig. 216). A metastatic tumor involved several of the vertebrae, while a fungating mass penetrated the spinal muscles and spread out beyond them as a sessile tumor. The joint

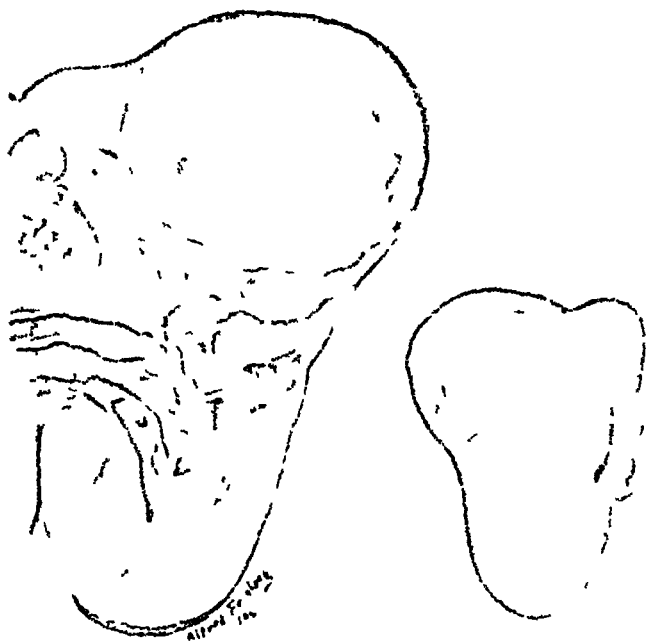


Fig. 217—Left kidney. Note hypernephroma mass with areas of necrosis.

surfaces and cartilages were intact, the margin was lobulated, and showed a distinct capsule.

There were no necrotic areas in the metastasis, which was pink in comparison to the primary growth. The prostate was not enlarged, the gastro-intestinal tract was normal. The microscopic examination of the tumor confirmed the diagnosis of gross examination (Figs. 218-219).

This leads me to discuss briefly the origin of these tumors, which has been the subject of dispute ever since the views propounded by Grawitz in 1883 were disputed by Sudeck in 1893. Ewing quotes Grawitz as believing that these tumors arise from adrenal rests or remnants in the kidney, and his arguments were that the tumors are located under the capsule where adrenal rests are found, the character of the cells, which are different from renal epithelium in their high content of

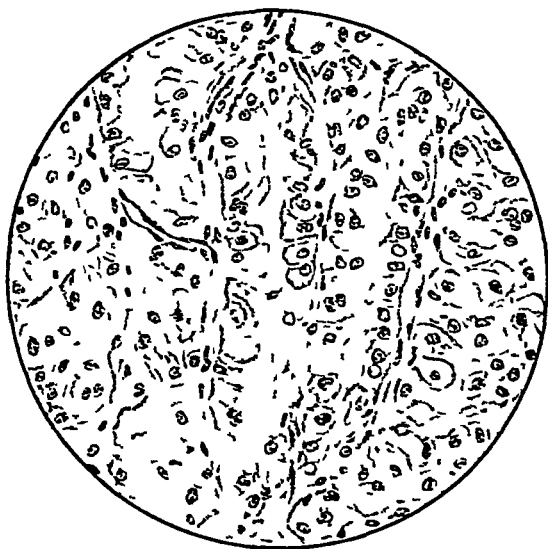


Fig 218 —High-power drawing of primary growth Hypernephroma Note the tubular arrangement of the cells

fat without evidence of degeneration the sharp encapsulation from the renal parenchyma, the resemblance of the structure to that of the adrenals, and the presence of small tumors with a fibrous core and a more cellular glandular cortex. Ewing believes that some of these tumors arise from adrenal rests and some from renal tissue, and lays most stress in differentiating them, upon the tubular character, with apparent lumina assumed by some of the tumors. Our tumor shows this characteristic structure and it is probably of renal origin (Fig 218)

The subject of treatment has not been stressed. If the diagnosis had been made before the metastasis occurred it might have been possible to have excised the tumor successfully. After the metastasis occurred radium might have been employed either superficially or by implantation of radium.

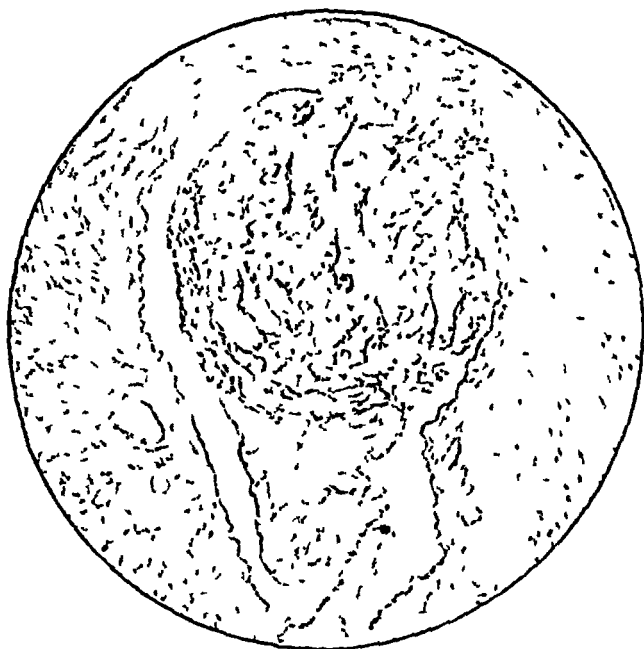


Fig. 219 —High power drawing of metastasis. Note lobular arrangement of cells and marked vascularity of tumor.

emanation in tubes, and x-ray in massive doses might have been applied. In the similar case which has come to my attention the kidney tumor was excised and radium was administered to the bone metastasis in the scapula, yet the patient died shortly after the operation.

A CASE OF ACUTE THYROIDITIS¹

ACUTE inflammation of the thyroid gland is not uncommon. In the literature it is referred to as "cynanche" or "angina thyroideæ," as "struma inflammatoria," "thyreophyma acutum," and "inflammatio glandulæ thyroideæ." The best name is "acute thyroiditis" a normal gland is involved and not a goiter.

The patient observed was an automobile mechanic, thirty-one years old, a native of the United States. The chief complaints were pain and swelling of the throat, with great difficulty in swallowing. The patient had had measles, scarlet fever, and tonsillitis in childhood, pneumonia four years ago, influenza seven years ago, and occasionally tonsillitis since then. There is no history of venereal disease. Until the present illness his appetite has been good and his bowels regular. He does not use alcohol.

Five days before the onset of the present illness, in November, 1921, while working under an automobile—lying on his back on the ground—he was squeezed by the running board of the car. A red mark was left on his chest. A few hours afterward his throat became sore, the swelling at first was in the region of the tonsils. He had several chills and some fever. For the past two days he has had great difficulty in swallowing, his neck has been swollen, and it is painful for him to speak.

Physical Examination—A white, well-developed man appears acutely ill. He is restless and evidently in pain with each swallowing motion. His teeth are in fair condition, the mucous membranes of his throat are red, the tonsils are enlarged, and there is pus exuding from the follicles. The left tonsil is more inflamed than the right. The anterior cervical lymph-nodes are inflamed. The larynx is apparently normal. The upper portion of the pharynx is moderately congested. There is a horseshoe-shaped swelling corresponding to the thy-

¹ From the Medical Service of Harlem Hospital, Dr L. K. Neff, Director

roid (Fig 220) The right lobe is larger than the left The thyroid is tender to touch, and when the patient swallows his saliva the thyroid is raised with the trachea, and this evidently causes great pain His heart shows no enlargement, murmur, or



FIG 220 —Enlargement of the thyroid in acute thyroiditis

arrhythmia, the sounds are normal The abdomen is normal The liver and spleen are not felt The skin shows no abnormality Excepting the anterior cervical lymph nodes, there is no enlargement There is no tenderness of the bones or joints Reflexes are normal There is no change in sensation other

than hyperalgesia in the anterior triangle of the neck. The patient's temperature was 102° F. on admission and rose to 104° F. The pulse was 110 on admission (Fig 221). The urine was amber, specific gravity 1024, acid, with heavy precipitate of albumin, no glucose, a few hyaline casts. A blood-culture was taken and found negative. Leukocyte count 17,000, polymorpho-

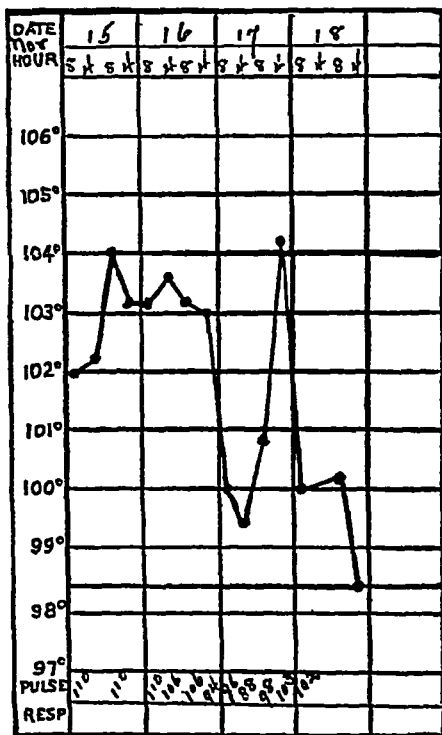


Fig 221

nuclears 83 per cent, lymphocytes 17 per cent. His blood-pressure was 115/80.

An ice-bag was applied to the patient's neck.

After four days the temperature had fallen to normal, the swelling of the gland had subsided, and the patient left the hospital.

This patient illustrates a combination of the usual causes of the trouble injury to the neck and a bacterial invasion following exposure

The outstanding features were the difficulty in swallowing and the dysphonia, from which the patient found considerable relief by lying prone with a gauze drain in the mouth so as to remove the saliva, thus obviating the necessity for swallowing, with consequent elevation of the thyroid and the attendant compression between the fasciæ of the neck

CLINIC OF DR BRET RATNER

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RABBIT HAIR ASTHMA IN CHILDREN*

IN the many contributions to the literature on protein sensitization only the most casual reference is made to rabbit hair as an etiologic factor in the production of asthma

Sporadic cases are cited of laboratory workers who get attacks of asthma when working with rabbits, and individuals whose attacks are precipitated by contact with pets Blackley, in 1873, reports the first case in the literature of a man aged fifty-four, who since the age of seventeen showed symptoms of asthma whenever in the presence of rabbits Recently Freeman tells of a case of "a man who has always hated the presence of rabbits, or rabbit meat, or rabbit skin he is devoted to shooting, but always has to get the keepers to put him where there have not been rabbits about, otherwise he knows he will not hit a bird" In all these cases it has been the direct contact with the animal that has brought about the reaction

Vander Veer, however, in his article on "The Asthma Problem" in 1920, cites the only case that we have been able to find in the literature of asthma which was caused by rabbit hair found in the pillows on which the patient slept. He states that this is an extreme case, but from my experience it would appear that rabbit hair is a rather common offender, its uses being manifold This phase of hypersensitiveness to rabbit hair is one of great practical significance, but it has not heretofore been emphasized

* Pediatric Department, N Y Nursery and Child's Hospital (Dr Jesse F Sammis, Director), and the Department of Pediatrics, Cornell Medical College (Dr Louis C. Schroeder, Acting Director)

Case I—A boy five and one-half years of age was referred to our clinic more than a year ago suffering from asthma. His family history was absolutely negative for any form of protein sensitization. The child had been perfectly well up to six months of age, from that time on he suffered from repeated attacks of coryza, and at the age of one year (after the family moved to Coney Island) he developed his first attack of asthma. He continued to have these attacks, and during the year prior to admission they had become more frequent and more severe. They were invariably preceded by running nose, sneezing, watery eyes, and cough. These prodromata would last for about a day, and at night his asthmatic attack would precipitate, with a gradual subsidence after two to three days. Vomiting and loss of appetite attended all attacks.

The mother insisted that it was something in Coney Island which caused these attacks because the child had never suffered from asthma before they moved there, and whenever she visited with him in Albany or Hudson he was free from attacks. Inasmuch as there was no history of eczema or gastro-intestinal disturbance it was felt that some keratin or animal hair was at the source of this case. The child was then tested repeatedly with all proteins we had on hand (rabbit hair was not one of the stock proteins at that time) and suggestive reactions were given by horse dander, chicken feather, cat hair, and dog hair. Further tests and investigations finally proved them absolutely negative. The child continued to have his attacks, however, and they became more frequent and more severe. But we could do nothing further and this case had to be classified as unsolved.

Several months later the child in one of his severe attacks contracted bronchitis and was advised admission into the hospital. He made a very rapid recovery of both his bronchitis and asthma. Upon the night of his return to his home he promptly developed another severe attack which lasted for three days. A week later I was hurriedly summoned to the child—this was my first home visit. I found the child at the height of a most intense attack, this time with a high tempera-

ture, chills, and attacks of cyanosis. There were suggestive signs of pneumonia. I was astonished to note on the blanket covering the child a great many small hairs. I immediately ordered the child to another room, and opened all the pillows, the mattress, and comforter. They all contained what appeared to be rabbit hair, and I told the parents that we had probably finally discovered the cause of the child's asthma. The child, who was suffering markedly in the next room, was taken up to the garret, which was the only place which seemed free from this ubiquitous rabbits' hair. The condition cleared up, and the child, after the house was thoroughly cleaned, was free from attacks. Strangely enough on the night before moving from Coney Island they stopped in a small hotel in the vicinity. The mother immediately inspected the pillows in her room and, to her mortification, discovered rabbit hair in them. She did all she could to prevent an attack but without avail, however, the attack was mild.

Several days later I tested the boy, and he gave positive reactions to the cutaneous test with the hairs removed from the pillows, and with the protein extract prepared by the Arlington Chemical Company. To further prove to the mother that the child was sensitive to rabbit hair, I took the child to the laboratory and gave him a rabbit to play with. After five minutes he began to complain that the room was getting very close, to rub his nose, and then sneeze. I asked him to play with the rabbit more vigorously, to run after it, and pull its fur. He again sneezed, rubbed his nose, and his eyes became watery. His breathing by now was extremely heavy and he felt very sick, this state became progressively worse, and in a few minutes he developed a typical severe attack of asthma. The entire sclera of the right eye became congested, the conjunctiva and eyelid markedly edematous, giving a beautiful picture of angioneurotic edema. Upon examination a rabbit hair was found in the eye. A hypodermic injection of adrenalin promptly relieved the asthma and eye condition, but the asthma recurred that night in a mild form.

This child has been under my observation continuously

and has been free from attacks, except once or twice when we have been able to trace them to attempts at desensitization, or contact with bedding containing the rabbit hair.

This case was so impressive that I immediately sent word to three other patients who repeatedly gave negative reactions to the various proteins. To my surprise, all were positive to rabbit hair.

Case II—Boy aged nine and one-half years, who was admitted to the clinic about one year ago suffering from asthma. Family history absolutely negative for protein sensitization. Since his early infancy, the mother states, the child had attacks of what might have been asthma. She used mustard plasters, etc., to relieve him, and as far back as she can remember he has always suffered from coryza and recurrent bronchitis. Mother dates his first real attack at about one year of age. Asthma has been repeatedly diagnosed at different hospitals since then.

Attacks usually started with a dry cough and almost invariably precipitated between 12 and 1 A. M., they generally lasted for two to three days, during which time the child would vomit his food and feel generally sick. They occurred perennially, once every week or two. They have, however, become less frequent, now occurring every five or six weeks.

The mother attributed his attacks to eating candy and running around on the street, coming into the house all tired out. However, after going through the gamut of our proteins we could not locate the source of his trouble. After our find in Case No. 1, as I have stated, we tested this boy with rabbit hair, and were rewarded with a positive reaction.

I then questioned the mother about her pillows. She was quite certain that they were filled with goose feathers, and stated that the child had slept on them from birth. But the following day she returned with a bag full of rabbit hair obtained from the pillows. I took some of this hair, had the child breathe it in, and rubbed some into his nose. While he did scratch his nose and sneeze no asthmatic attack ensued. A little disappointed, I took the boy to the animal house, as I had done

with No 1 The child held the rabbit in his arms and shook the fur After five minutes his eyes blinked and he began to sneeze His eyes became watery, nose itchy, with a slight mucous discharge By now asthmatic wheezes were heard in the chest, but no attack developed However, I told the mother to be sure to discard the pillows that night The next day the mother telephoned to advise me that the child had had an extremely severe attack following his return from the hospital

With the exception of several attacks this past summer which were discovered to be due to pillows filled with rabbit hair, which were brought out by a friend who was sharing their room, this boy has been free from asthma He is still, at this writing, under my observation

Case III—A boy aged seven years Family history is negative for asthma, etc For the first two years of his life the child was perfectly well At the age of two the family moved from Brooklyn to Providence, where they lived at the home of the grandmother Upon his arrival he contracted a cold, developed diphtheria, and two weeks later pneumonia He was in the hospital three weeks, dangerously ill However he recovered, and was brought home in a very weakened condition A week after his return from the hospital he developed asthma

He then moved to New Bedford to live with the mother's sister, where he had repeated attacks occurring every two weeks They were always preceded by sneezing, coughing, and suffusion of the eyes, asthma would then set in and last for three days The child always complained of pains in the stomach region and would vomit a great deal The mother then lived with another sister in Providence for several months, and there the child was free from attacks

Upon his return to New York the attacks recurred and continued As in the other two cases, all tests reacted negatively until we tried the rabbit hair The home was carefully investigated, but no trace of rabbit hair was found in pillows or other bedding In this case it was the father who was at fault He was employed in a men's hat factory, and his duties

were to rub down the rough felt with pumice. Investigation revealed a tremendous amount of finely broken up hairs on his clothing and person. A letter from a Danbury hat factory stated that rabbits' fur was used in the manufacture of practically all felt hats. Dust from the father's factory was extracted and gave a positive skin reaction in this case and all the other cases of rabbit hair hypersensitiveness.

This child, too, was given a rabbit to play with, but developed no reaction until four hours later. It is interesting here to note that this child gave the greatest skin reaction of any of the cases, and showed the slowest clinical response. The attack lasted for two whole days and adrenalin injections gave only temporary relief.

The mother visited the homes in Providence and New Bedford, and returned with rabbit's hair from the pillows. The pillows in the home of the sister where he had been free from attacks, however, contained goose feathers.

The father has been advised to take greatest precautions to remove all the factory dust after a day's work. The child still continues, however, to have occasional attacks which are probably due to the factory dust.

Case IV — A boy of seven and one-half years at the time of admission in whom the same situation prevailed as in the former cases gives the following history. The mother dates the first attack of asthma from eight months of age and from earliest infancy the child has had coryza and bronchitis. He has practically never been free from attacks, and the intervening times between attacks he always suffered from chronic coryza. His attacks also lasted from two to three days and the child also vomits during attacks and suffers loss of appetite.

The search for rabbit hair was very discouraging, but the offending pillow was finally located. He had used this since birth. When it was opened much of the contents floated into the room and the child developed an attack of asthma. A clinical test with a live rabbit resulted similarly to the other cases but this child, in addition, developed large urticarial wheals wherever the hairs rubbed against the face or body.

This child has improved tremendously since removal of the pillows, but has suffered from several attacks in the past year, which were directly traced to rabbit's hair at a neighbor's home

Case V—A boy aged fourteen who had had asthma for the past two years was being treated by a colleague, for foods to which he reacted, but he continued to have attacks which invariably came out at night throughout his course of treatment. This doctor had obtained a reaction to rabbit hair, but it was disregarded inasmuch as no pets were found at home, and the mother had brought samples from the pillows, which all contained feathers. When the boy was admitted to the hospital recently, however, suffering from his most severe attack, I had occasion to test him. I found the reaction to rabbit hair. I immediately went to the boy's home and discovered that a large comforter used in the boy's room was filled with rabbit's hair—thus the family possessed for two years. The boy has been free from attacks since this has been discarded.

Case VI—A boy aged nine years came to the clinic a year and a half ago (before the aforementioned cases had come to my notice). The child at that time reacted to lactalbumin and beef. After our initial studies this case was lost sight of. During the period of absence the child suffered continuously from asthma, the attacks coming on usually at night. Before taking any further steps I requested the mother to bring me samples of the pillows and other bedding. Three of the pillows contained rabbit hair. A cutaneous test was made with these hairs and the regular rabbit hair protein (Arlington), and in both cases positive reactions were obtained. It might be interesting to note that the child had asthma for the past six years and the pillows had been in the possession of the family six and one-half years.

Case VII—A girl aged five. Father a hay-fever sufferer. Last winter the child suffered from colds continuously. This year still suffered from coryza, but to a much less extent. I was attracted to the child's hat, which was made of rabbit fur. I noted that the hairs flew off easily. Upon further questioning was informed that last year the child had worn an entire coat

made of the same fur. The mother noted that the hairs were easily shed, and therefore discarded the coat this winter. A cutaneous test for rabbit hair revealed a positive reaction, and I advised discarding the fur hat.

Case VIII—A child twenty months old, who since infancy has suffered from coryza and recurrent bronchitis, has had about six attacks of asthma this past year, gave a positive skin test to rabbit hair. A visit to the home revealed a large pillow filled with the hair which was used only occasionally. Upon questioning the parents the father recalled that the previous summer when the child played with a rabbit he got a severe attack of asthma. This occurred in the country and the family immediately returned to the city. No importance was attributed to this at the time. The fact that the pillow was used only occasionally accounts for the infrequency of the attacks. I might bring out a further interesting fact: this pillow was given the family by an aunt who has since died of tuberculosis and who had always suffered from asthma.

Discussion—There is a specificity about protein sensitization that commands the respect of all who work in this field, and when a positive skin test is obtained, the physician should leave no stone unturned to locate the offending protein. There was no suggestion given in the histories by the parents of what the cause of the asthma might be, and it was only after having visited the home of Case No. 1 that this type of case was brought to our attention, and there is every indication that many such cases exist, judging from the varied uses that rabbit hair is apparently being put to.

A hair placed on the eyeball or the hair rubbed into a scratch in the skin with or without tenth-normal sodium hydroxide will give a positive reaction. Inhalation of the hair will precipitate an attack the same as exposure to the animal will, so that the diagnosis can be made without difficulty.

While we cannot as yet say anything definitely about our attempts at desensitization, the simple and satisfactory method of treatment is the thorough removal of all the hair.

Walker states "that asthma in infants and very young

children frequently presents at first a condition of frequent colds or bronchitis even though the cause is anaphylactic in nature and not due to bacterial infection. This is probably so because the infant's bronchial mucous membrane and respiratory mechanism is easily irritated. Furthermore, since such a young individual spends most of its time sleeping by itself it is possible that he can have true attacks of bronchial asthma long enough to produce a constant bronchitis before the immediate family might recognize any ailment." Missildine, in studying several cases of horse asthma in children, also finds that children who are subject to the phenomenon are apt to go several years without the cause being associated with the horse, but rather with the more familiar causes of rhinitis.

My experience concurs with the above writers, as practically all of the children complained of repeated colds and recurrent bronchitis before the asthma developed. A probable mechanism for the development of asthma therefore suggests itself in these cases. The delicate, easily irritated mucosa of certain infants, continually coming in contact with the rabbit hair, gradually becomes congested and more permeable. This allows for the absorption of the protein into the system. Specific rabbit hair antibodies may then be formed and anaphylactic phenomena follow, with asthma as the clinical manifestation.

Infants with repeated colds and recurrent bronchitis should be regarded as potential asthmatics, and every effort at preventive measures instituted at this stage. I would therefore suggest that all infants should be permitted to sleep only on pillows filled with silk floss, and that all feathers and short, dust-producing, easily shed hairs be kept from them.

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CLINIC OF DR HERMAN O MOSENTHAL

POST-GRADUATE MEDICAL SCHOOL AND HOSPITAL

THE TREATMENT OF HIGH BLOOD-PRESSURE

A BLOOD-PRESSURE that is higher than normal may occur as a symptom of nephritis, certain cerebral disturbances, nervous excitement, aortic insufficiency, and of other conditions. If all such symptomatic hypertensions are excluded there remains a far greater number whose supernormal blood-pressure cannot be explained on clinical grounds. These cases have been variously named essential hypertension, hypertensive cardiovascular disease, hyperpiesis, etc. Objection has been made to these terms because they do not adequately describe the disease. This criticism is perfectly correct, in answer, however, it may be stated that these names are honestly conceived, because at the present time we know nothing more than the fact that hypertension may exist without known cause and without accompanying symptomatology or pathology of any kind. It is the treatment of this malady which we wish to take up this morning. Every one does not agree with all of the above statements, especially in relation to our lack of knowledge in regard to the causation of essential hypertension. It is very necessary that we should have as clear an understanding as possible concerning the causation and mode of production of this condition, for it is only upon this basis that we can agree upon the proper therapy for it. Hence these questions should be carefully considered at this time.

Some Facts Regarding the Relation of the Kidneys to Essential Hypertension—In 1836 Richard Bright observed that cardiac hypertrophy and dilatation were often present in nephritis. Such changes in the heart have been and are still

considered to indicate that an increased blood-pressure existed during life. This conclusion is correct in the majority of instances. There are some cases of marked cardiac hypertrophy and dilatation that occur in adults and occasionally in children without apparent cause, the so-called idiopathic cardiac hypertrophies, that may for the moment be disregarded.

If we study the relationship of hypertension to nephritis from another angle, that is, during life, instead of at the autopsy table, we find that when the blood-pressure is raised above the normal a nephritis of some sort or degree is almost certainly present. Coupling these two corroborative facts as developed by the clinician, on the one hand, and the pathologist, on the other, it is evident that kidney disease and hypertension are closely related to one another. Thus far our reasoning has been perfectly sound. If in the joy of acquired knowledge we now recklessly assume that every instance of hypertension is secondary to kidney involvement, we are taking unwarranted liberties with the facts at our command. However, this is precisely what has been done, and has led to the belief that an increased blood-pressure is an inevitable sign of Bright's disease, this idea was firmly adhered to until about fifteen years ago, today it is still unduly honored, but not to the same extent.

It is worth while to pause for a moment and take stock of our precise knowledge, clinical and experimental, of the relation of the kidney to blood-pressure. The pivotal idea has always been that a diminished excretory activity of the kidney results in efforts intended to restore normal renal function. Among these changes an increase of arterial pressure is considered to be one of the most important. A great deal of evidence both for and against this theory has been developed.

In animal experiments it has been demonstrated that a reduction of kidney substance results in an increase of blood-pressure (Janeway, Pissler, and Heinicke). A total removal of both kidneys, however, does not bring this about. This curious fact has its counterpart in clinical medicine. Prostatic hypertrophy with its attendant, mechanical interference with

urinary elimination, often results in a rise of arterial pressure (O'Connor, Monakow and Mayer) The blood-pressure has a tendency to return to a normal level when the urinary flow is again properly established by a retention catheter or operative relief Complete anuria, on the other hand, leaves the blood-pressure comparatively unchanged This is well illustrated when a fatal termination is brought on by complete suppression of urine in bichlorid of mercury poisoning when the blood-pressure remains unchanged, there are occasional exceptions to this rule, because of their rarity such cases have been treasured, Janeway and Volhard have reported examples of this sort in which there was a very moderate increase in arterial pressure It is evident that there is a distinct relation between urinary flow and hypertension, but that there is not a mathematic increase in the latter as the former progressively diminishes There must be another element in the situation that has not been satisfactorily determined We can approach the problem a little more intelligently if we are able to grasp the vascular mechanism that is responsible for hypertension

The Part Played by the Vascular System in Producing Hypertension—There are two factors concerned in maintaining the arterial blood under pressure These are the volume of blood injected into the arterial reservoir with each heart-beat and the tonicity of the arteries, both large and small The character of the heart-beat may be considered as the main element determining the systolic pressure, the tonicity of the arterioles controls the diastolic tension

When the heart is not beating, that is, during diastole, the degree of arterial pressure depends principally on the tonicity of the arterial wall It is clear that in a rigid system of pipes with a pump causing an inflow of fluid at one end and an outlet provided at the other an increase of pressure of the contained fluid occurs only when the pump exerts its force, if this ceases the inelastic walls of the system allow the contained fluid to remain at a zero pressure This state of affairs is approached in conditions of arteriosclerosis, when the blood-vessels become hard, lose their elasticity, contractility, and

consequently their tonicity. The diastolic pressure in such cases must fall below the normal level and the systolic rise, since the blood propelled by the heart meets an unyielding resistance. In former years, before the diastolic blood-pressure was as much studied as it is today, "hardening" of the arteries was considered to be one of the main causes of hypertension. Today we know that very extensive sclerosis of the arteries may exist without very much change in the blood-pressure. This is a matter of clinical observation. These cases are the ones in which the sclerotic process in the blood-vessels has been a primary one. There is another group of patients in which hypertension and thickened arteries occur simultaneously, this is far the more frequent type. In this instance the strain imposed by the increased blood-pressure has brought on the degenerative changes in the arteries. If rigidity of the blood-vessels—arteriosclerosis—lowers the diastolic arterial pressure and raises the systolic but slightly, where are we to seek for the cause of hypertension?

An increased blood-pressure is not a constant phenomenon, as is shown in Figs 222-224. In these charts it is evident that the degree of variation that occurs is fairly large. This variability of arterial tension furnishes a clue as to the nature of high blood-pressure. There can only be one factor responsible for it under the circumstances, and that is an augmented muscular action on the part of the heart and the blood-vessels. When the tonicity of the arteries is increased the diastolic pressure must rise, for the blood is then held under greater tension than usual throughout the cardiac cycle. It follows, of course, that the systolic pressure increases as well for the heart forces the blood into a reservoir which presents a greater resistance that must be overcome if the circulation is to be maintained. It has frequently been assumed that such a tonic state of the arterial musculature is the sole factor responsible for hypertension, if this were so the diastolic and systolic pressures should vary in constant proportion. This is not the case. The following data taken from a number of patients may furnish evidence to substantiate this statement (Table 1).

TABLE 1

SHOWING THE VARIOUS RELATIONS THAT MAY EXIST BETWEEN SYSTOLIC AND DIASTOLIC BLOOD-PRESSURES

Blood-pressure.		Remarks.
Systolic.	Diastolic.	
230	92	Group No 1 Examples of comparatively low diastolic pressure and markedly increased systolic pressure
184	90	
220	98	
180	95	
225	94	
200	96	
234	134	Group No 2 Examples of simultaneous increase of systolic and diastolic blood-pressure
232	132	
200	130	
245	140	
280	136	
230	135	
170	120	Group No 3 Examples of increased diastolic pressure with a comparatively slight rise in systolic tension, these cases are comparatively rare
177	120	
161	120	
190	130	
170	110	

From Table 1 it is apparent that the systolic pressure usually rises more in hypertensive disease than the diastolic, and when the increased blood-pressure diminishes the systolic drops much more than the diastolic (Fig 222) These facts make it evident that the force of the individual heart-beat is likely to vary independently of the state of arterial tone

The variations in diastolic pressure indicate the degree of tonicity in the arteries This is not necessarily increased in hypertension, which may affect only the systolic pressure as shown in Group No 1, Table 1 On the other hand, in the rather uncommon cases in which the diastolic pressure is disproportionately raised as compared to the systolic tension it is evident that the function of the arteries is mainly disturbed, and that of the heart scarcely at all

We may conclude, therefore, that two factors are concerned in the production of hypertension, the increased force of the heart-beat and the pathologic degree of tonicity in the arteries, and that to a great degree these elements act independently of one another

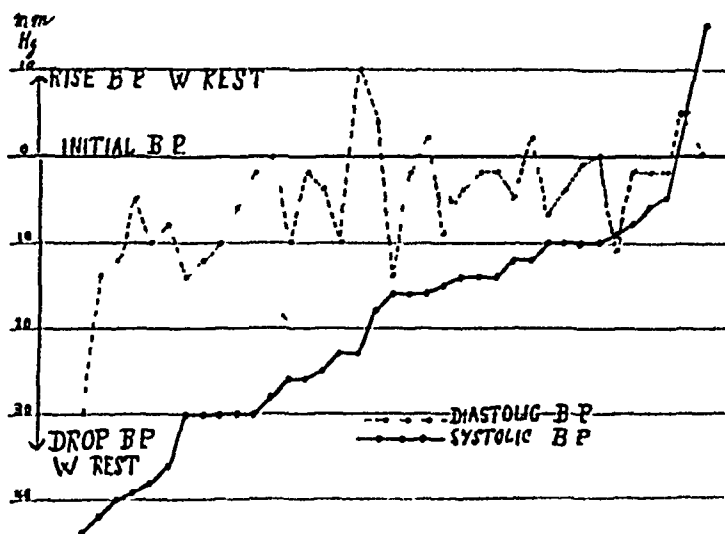


Fig. 222—Variation of systolic and diastolic blood pressures from the initial pressure on lying down (short periods of rest) in hypertensive patients (systolic blood pressure of 160 or higher). The horizontal line marked 0 represents the initial pressure. Every vertical pair of dots represents the greatest drop recorded in each case. The distance below the line indicates the amount of drop obtained. The systolic readings of the various cases are connected by a solid line, the diastolic, by a broken line. The observations are charted in the order of degree of drop in the systolic pressure.

The variations are decidedly less in the diastolic than in the systolic pressure. The drop in diastolic pressure, except in the first case, is so slight that it does not appear to be of great clinical significance. This is in marked contrast to the changes that occur in the systolic pressure, which often shows a very great fall on resting.

The Cause of the Increased Heart Action and Tonicity of the Arterioles in Hypertension—It is well established that nervous influences cause the blood-pressure to rise and fall in a most bizarre way. O'Hare and Boys have called attention

to this fact recently. In Figs 222-224 are given the results obtained by short and more prolonged periods of rest. It is perfectly evident that within a brief space of time, fifteen minutes to one hour, relaxation brings about a drop in blood-pressure (Figs 222, 223), if the stay in bed is prolonged over a period

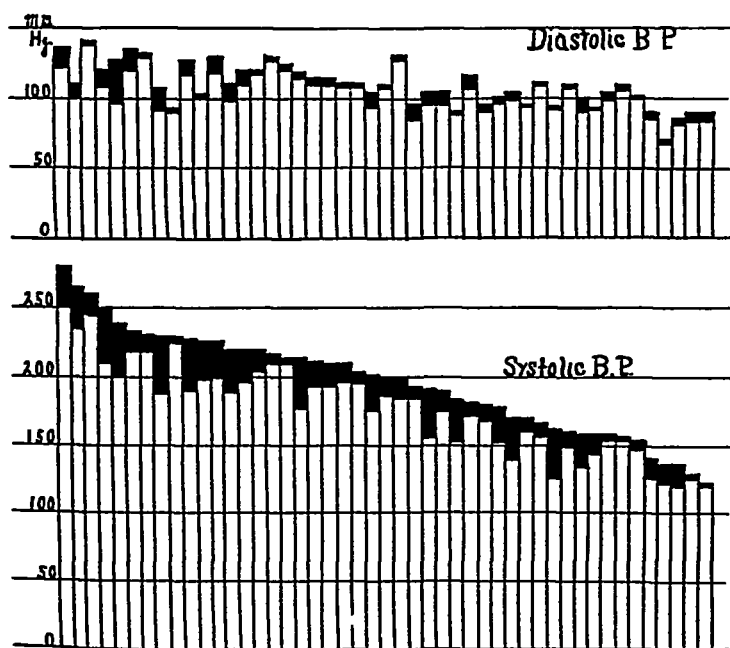


Fig 223 —Drop in blood-pressure obtained with short periods of rest. The lower columns represent the systolic blood-pressure, the superimposed upper column, the diastolic blood-pressure in the same patient. Each set of columns corresponds to a different case. The entire column represents the initial blood-pressure, the dark portion of the column indicates the drop in blood pressure which occurred.

of several days the diminution in blood-pressure is much more marked and the normal level is approached in many instances (Fig 224). The drop in tension affects both the systolic and diastolic pressures, though the drop in diastolic pressure is not as constant nor as great (Fig 222). Such observations make it certain that the release from overactive nervous impulses

affects both the action of the heart and arterioles favorably, and inasmuch as the systolic pressure undergoes the greater improvement it is only fair to surmise that the heart is more readily influenced than the arterioles. All these facts are of great importance in directing the treatment of these cases, and will be taken up a little later.

At this point I wish to accentuate one fact, which may be gleaned particularly from the marked fluctuations in the blood-

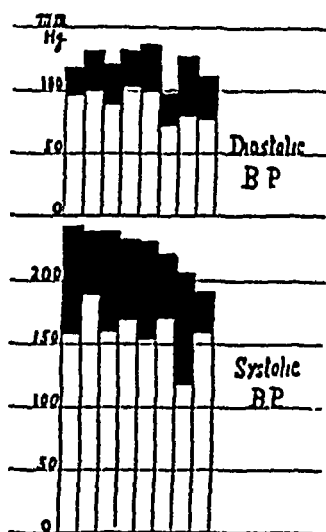


Fig. 224 — Drop in blood pressure obtained over a period of several days rest in bed. The columns and their dark areas have the same significance as those in Fig. 223. The diminution of blood pressure is much greater with prolonged rest than it is in shorter periods of quiet, as a comparison with Fig. 223 shows.

pressure shown in Fig. 224. Hypertension is apparently not a compensatory factor that cannot be dispensed with, the patients shown in Fig. 224 were as comfortable and as symptomless when the blood-pressure was low as when it was high. Hence the idea, prevalent some years ago, that an increased arterial tension should not be interfered with because it was a compensatory exaggeration of function necessary to maintain the well-being of the individual does not appear to be correct, and

we are at liberty to lower the blood-pressure as near to normal as possible without causing any harm

Why Should Hypertension Be Reduced?—If an increased blood-pressure causes no symptoms, why should attempts be made to lessen it? A rise in arterial tension in itself does no harm, but if it continues indefinitely it results in certain changes that are of vital importance to the patient. These are

1 Cardiac hypertrophy and dilatation, and finally myocardial insufficiency

2 Cerebral arteriosclerosis, entailing changes in the brain, especially hemorrhage

3 Arteriosclerosis of the renal vessels, resulting in primary contracted or arteriosclerotic kidney

The three sets of changes mentioned above are not the only ones that commonly occur, but they are the usual three vital processes that are the sequels to an increased blood-pressure. This must be recognized, for if the hypertension cannot be controlled, then prophylactic treatment must be instituted to forestall as far as possible the development of symptoms from its almost inevitable complications.

It is of distinct help in the regulation of the treatment of essential hypertension to know which of the three organs—heart, brain, or kidney—is most likely to be involved. Thanks to the statistics of Theodore Janeway and others, which I believe anyone who practices internal medicine will be able to affirm from his clinical experience, myocardial insufficiency is the usual cause of death in these patients, next in frequency is the occurrence of cerebral complications, and last and by far the least common is uremia induced by deficient activity of the kidney. The actual percentages of the causes of death in Janeway's series were as follows

<i>Cardiac</i>	Cardiac insufficiency	35.0	} 46.7 per cent
	Angina pectoris	7.3	
	Edema of lungs	4.4	
<i>Uremic</i>	Convulsions, coma, or gradual uremia	22.6 per cent	
<i>Cerebral</i>	Apoplexy or its results	14.6 per cent	

(It is freely acknowledged today that many of the cases that have been diagnosed as uremia are, in reality, due to the changes accompanying cerebral arterio-sclerosis. A study of renal function by more modern methods has revealed this fact. It is probable, therefore, that the above figures should show a higher percentage of deaths due to apoplexy and its results and a lower mortality from uremia.)

It is interesting to note how completely this more modern conception of hypertension differs from the older views in regard to it. Formally an increased blood-pressure was supposed to be secondary to the "small red kidney," now we are certain that the primary contracted kidney develops as the result of a hypertension, and that in most cases a fatal termination does not depend upon the renal involvement but upon the heart.

THE CONTROL OF HYPERTENSION

has been attempted in many ways. None of them have been completely successful, some of them rest upon hearsay and tradition rather than upon clinical observation. Something may be accomplished along these lines in certain cases. However they cannot be treated as a group, but must be studied individually, as the subsequent discussion will attempt to show.

The Effect of Protein in the Diet—For many years protein foods were considered to be at the root of the "blood-pressure evil." The dietary prescription of meat once a day or less and as few eggs as possible has been advocated until the meatless diet has become a popular slogan. There is no doubt about the fact that many of our citizens through an overindulgence in starchy foods are becoming obese and favoring the development of "high blood-pressure" and "hardening of the arteries" by the very diet that is supposed to prevent these maladies.

The feeding of protein, as meats or otherwise, will not tend to increase the blood-pressure of a hypertensive individual. The following case (Table 2) taken from a series of such observations¹ will demonstrate this.

¹ Mosenthal H. O. *Am. J. Med. Sci.* 1920 clx, 893

TABLE 2

Blood-pressure observations in a case of hypertension (Male, aged sixty-seven years Secondary contracted kidney, at times a trace of albumin and a few hyaline and granular casts a phthalein excretion of 25 per cent in two hours and ten minutes, urea nitrogen, 34 mg per 100 c.c. of blood moderate arteriosclerosis) There is no notable change in the level of the arterial pressure on a high or a restricted protein intake, while the total number of calories is maintained at a constant level

Day	Blood-pressure		Diet		Character
	Systolic	Diastolic	Protein gm	Total calories	
1	190	120	91 (28) ¹	2344	Normal diet
2	175	105	86 (19)	2498	
3	195	115	80 (28)	2501	High protein
4	190	110	125 (69)	2065	
5	178	112	125 (74)	2065	
6	194	120	125 (75)	2065	
7	183	125	125 (76)	2065	
8	188	115	125 (76)	2065	
9	187	119	125 (69)	2065	
10	190	116	125 (79)	2065	
11	170	103	125 (64)	2065	
12	175	105	125 (80)	2065	
13	195	108	125 (78)	2065	Restricted protein
14	182	104	125 (68)	2065	
15	185	113	125 (76)	2065	
16	187	107	125 (80)	2065	
17	175	115	125 (72)	2065	
18	194	109	50 (18)	2065	
19	181	109	50 (16)	2065	
20	178	100	50 (29)	2065	
21	173	103	50 (18)	2065	
22	209	114	50 (29)	2065	
23	178	105	50 (16)	2065	
24	203	115	50 (11)	2065	
25	188	117	50 (16)	2065	
26	173	106	50 (16)	2065	
27	183	110	50 (16)	2065	
28	182	110	50 (16)	2065	
29	182	110	50 (17)	2065	
30	190	115	50 (14)	2065	
31	206	125	50 (17)	2065	
32	190	125	50 (14)	2065	
33	210	120	50 (20)	2065	
34	195	115	50 (19)	2065	
35	201	115	50 (31)	2065	
36	185	115	50 (21)	2065	
37	205	110	50 (13)	2065	
38	205	105	50 (29)	2065	
39	202	112	50 (18)	2065	

¹ Figures in parentheses are the quantity of protein from meat or fish

There is another side to this problem of the relation of blood-pressure to protein food. If the protein constituent of the diet is either curtailed or given in excess over a long period, certain changes are brought about in the body's make-up that entail a lowering or raising of the blood-pressure. Benedict and his collaborators have shown that undernutrition brings about a secondary anemia, diminished vitality, and a lowered arterial tension, it must be borne in mind that the patient pays the price of lessened efficiency if this therapeutic goal is to be reached by these means. The physician must be the judge of how far these two factors may be balanced against each other in each case, and regulate the protein content of the food accordingly.

An increased number of red blood-cells may be accompanied by a rise in blood-pressure. This is true of some cases of polycythemia, but not of all. Why it should occur in some of these patients and not in others has not been determined. However, in certain instances a reduction of the protein food may serve to diminish the red blood-cells and at the same time to lower the blood-pressure. This is a matter that has not been studied sufficiently in clinical medicine, but it may possibly yield favorable results if it is tried out.

The former idea that the retention of the end-products of protein digestion act as irritants that stimulate the heart and the arteries to increased activity and raise the blood-pressure cannot be considered to be correct. Many of these cases do have a high blood-pressure, but its cause must be sought in another direction. Dietetic therapy in these instances demands a lowered protein intake, but while ordering it we must be clear in our mind that we are doing it to relieve the kidney of its burden and not to diminish the hypertension. A case with a high blood chemistry and a normal blood-pressure is the following:

D. K. Age twenty. Blood urea nitrogen 86.2 mg per 100 c c, blood uric acid 8.3 mg per 100 c c, and blood creatinin 5 mg per 100 c c, the urine contained a considerable amount of albumin and a few red blood-cells, the case was evidently a secondary

contracted kidney of marked degree, blood-pressure readings taken at various times were 132/80, 132/85, 136/85, 142/80, 148/80, 164/83, the two last were the highest readings obtained of a considerable number that are not charted, some of these observations were made during office visits when the blood-pressure would naturally show a tendency to be at its highest level because of the nervous tension involved

In regard to the use of proteins in essential hypertension it may be concluded that enough protein food should be allowed to maintain the body in an efficient condition, and that there is nothing to be gained by the routine restriction of meat, fish, or eggs. A deficient renal function in these cases may demand a curtailment of proteins for other reasons

The Effect of Carbohydrate in the Diet—The starches have always been considered the most innocuous of foods. Their final digestive products are carbon dioxide and water, which put no strain on any of the eliminative functions. This is all perfectly correct and deserves consideration in the dietetic therapy of many diseases. Today the amateur doctor advocates a high starch diet for himself and his friends to prevent high blood-pressure among a number of other ills. The one drawback to this mode of living is that it is prone to engender obesity in the individual who pursues this cult.

Many persons may become obese and exhibit no increase in their arterial tension, others are not so fortunate. If the combination of obesity and increased blood-pressure does exist, a restriction of the starchy foods may bring relief. In one patient the blood-pressure dropped from 146/88 to 112/72, while the weight diminished by 25 pounds. Dr W W Herrick tells me that by reduction of weight through regulation of the starchy element in the diet he was able to lower the systolic pressure from above 200 to normal in an obese woman.

In overweight individuals a control of the starchy food may, therefore, be of distinct importance in regulating the blood-pressure.

The Effect of Fats in the Diet—What has been said in regard to the relation of starches to obesity and hypertension may be

repeated for the fatty foods. The fats in themselves appear to have no other specific effect upon the level of the blood-pressure.

The Influence of Sodium Chlorid upon Blood-pressure—In 1904 Ambard and Beaujard expressed the belief that salt retention resulted in an increased blood-pressure. Such an inefficient excretion of salt was supposed to be the result of nephritis and renal insufficiency. Various Frenchmen, especially Ambard, confirmed the above theory. Even in the published cases of these authors there is a considerable number that do not exhibit hypertension, furthermore, the very obvious fact has been pointed out that it is generally appreciated that those types of nephritis characterized by salt retention have as their outstanding features albuminuria, edema, and no increase in

TABLE 3

Cases demonstrating the lack of relationship between blood pressure and concentration of sodium chlorid in the blood. These were consecutive cases of hypertension. There are fewer cases exhibiting a sodium chlorid concentration greater than 500 mg. per 100 c. c. than a lower level.

Case	Sodium chlorid mg. per 100 c.c. whole blood	Blood pressure mm. mercury
1	627	226/90
2	588	184/110
3	557	208/94
4	538	221/120
5	519	180/76
6	500	211/136
7	500	200/82
8	500	212/130
9	494	224/120
10	494	224/106
11	488	206/126
12	482	156/100
13	478	216/132
14	478	210/114
15	475	210/116
16	462	246/120
17	450	230/115
18	429	201/128
19	429	170/110
20	429	224/126

blood-pressure Looking at the matter from the point of view of a kidney complication it would not seem that inability on the part of the kidney to excrete salt was productive of a rise in blood-pressure

The sodium chlorid in the blood may be high for a number of reasons If salt is a factor in bringing about hypertension it may be that its increased concentration in the blood is the factor that is responsible for a rise in arterial pressure This matter is easily determined because clinical material collected over even a very short period shows very definitely that no very close relation exists between blood-pressure and the concentration of salt in the blood (See Table 3) If we regard this matter from another angle and note the blood-pressures in cases that exhibit an unusual amount of sodium chlorid in the blood (Table 4) it is very evident that an increased amount

TABLE 4

Consecutive cases exhibiting an increased concentration of salt in the blood There is no direct relationship between the sodium chlorid and the arterial tension About one-half the cases exhibit a normal blood-pressure in the presence of a raised blood chlorid concentration

Case.	Sodium chlorid mg per 100 c.c. whole blood	Blood pressure mm. mercury
1	676	105/52
2	627	226/90
3	625	98/80
4	588	140/84
5	588	184/110
6	562	150/86
7	557	208/194
8	550	130/70
9	550	104/78
10	544	148/90
11	538	224/120
12	538	108/82
13	532	108/74
14	530	148/86
15	529	120/66
16	519	180/76
17	513	170/86
18	511	136/70

of sodium chlorid does not necessarily entail a rise in blood-pressure O Hare's experience in regard to the blood chlorids is very similar to that given above It is as follows

"An interesting sidelight is thrown on the subject by a series of 45 or 46 cases of hypertension These have been arranged according to the height of the maximum blood chlorid About 20 cases or a little under one-half showed normal blood chlorids These normal cases were largely cases of vascular hypertension, whereas those cases showing high blood chlorids were, on the whole, chronic nephritics, with retention of nitrogen bodies as well as salt Curiously enough, those cases that showed the normal chlorids averaged the higher blood-pressure "

Increasing or diminishing the salt in the diet in hypertension is, according to Allen, prone to be followed by a corresponding rise or fall in blood-pressure McLester and Strouse have failed to obtain the same Dr James Short and I, working in this clinic, have not succeeded in affecting arterial tension by the administration of 10 grams of sodium chlorid The detailed description of these observations I wish to reserve for another time The disastrous effect which this amount of sodium chlorid is supposed to have in cases of hypertension we have witnessed only once This was a patient who had a marked renal insufficiency In cases of essential hypertension unaccompanied by renal or other complications it is perfectly safe to administer salt as desired

From the above it appears that sodium chlorid does not affect the blood-pressure, and that no object is attained by putting burdensome restrictions in this regard upon patients suffering with essential hypertension That nephritis of any type may be accompanied by insufficient chlorid elimination must be borne in mind, the salt intake must be adjusted to the ability of the kidney to handle the situation and no attention need be paid to height of the arterial pressure

The Effect of Fluid Intake Upon Blood-pressure—No consideration of the effect of diet on blood-pressure could approximate thoroughness unless this subject were considered Recently

Miller and Williams reported the finding that there was a marked increase in arterial tension when huge amounts of fluid were drunk. This observation is extremely interesting, its clinical application, however, is another matter. When only such quantities of liquid are ingested that come within the range of clinical probability there is no rise of note in the blood-pressure, a large number of researches bear witness to this statement. Furthermore, the intravenous administration of any of the solutions commonly used up to 1000 c c and more apparently does not affect the blood-pressure. Most of us have watched patients during blood transfusion and failed to find any change in arterial tension as the result of this measure. It may be concluded, therefore, that it is not worth while to limit the quantity of fluids in the diet with a view to controlling blood-pressure.

Control of Blood-pressure By Relaxation—The previous methods given cannot be said to be productive of anything that may be considered to be a constant or reliable result in reducing blood-pressure. The only procedure that has been at all satisfactory in my hands as yielding a drop in blood-pressure that may be regarded as a definite effect of therapeutic interference has been nervous relaxation obtained by longer or shorter periods of rest.

Relief from nervous strain may reduce arterial tension. It is difficult to demonstrate this because we have no absolute way of measuring the amount of worry and anxiety a patient may be harboring at any one time. In addition, there is the other side of the problem to be considered, namely, the receptivity of the individual, responsibilities that make one man grow restless, nervous and unequal to his task, only serve in another to spur him on to greater activities without ruffling him in the least. It cannot be said without reservation that removal of nervous strain will lower blood-pressure because the matter is almost impossible of absolute proof under usual conditions. However, O'Hare has recently shown that conversing about worrisome topics will raise arterial pressure to an amazing degree, there are many impressions that this is correct, Dr

James Short, recently working in our wards was able to confirm O'Hare's results

One incident may serve to show how undue anxiety will increase the blood-pressure. An elderly gentleman, whose life was very methodical and free from almost any unusual interference, was in the habit of visiting me about once a month and have his blood-pressure determined. Over a period of several years it fluctuated between 170 and 190. At one time it reached 240, to return to its accustomed level a few weeks later and remain there. On investigation it developed that the patient's brother had been the subject of an exploratory laparotomy for what the attending surgeon had diagnosed as a carcinoma, the tumor proved to be a benign one and the recovery of the brother seemed assured. With the favorable turn of events the blood-pressure of our patient dropped. *

Occurrences of this sort indicate how vital it is to regulate the business and family cares of hypertensive patients. The difficulty of doing this with any degree of success is fully appreciated and demands an unusual amount of tact, co operation, and forbearance on the part of all concerned.

Rest over shorter or longer periods can be studied more satisfactorily than the intangible effect of nervous influences. O'Hare and Bois have recently done this, and have come to the conclusion, as have others, that relaxation in the recumbent position will diminish arterial tension. A series of cases is presented (Figs 222, 223) which demonstrates the same point.

There are several facts that should be noted if the full significance of these observations is to be taken advantage of. Figure 222 shows how great the drop in blood-pressure may be. A diminution of 10 mm. or more of mercury in the systolic pressure of 3 of the cases is proof of this. On the other hand, the effect upon the diastolic tension is decidedly less marked and ranges within comparatively narrow limits regardless of the fluctuations that occur in the systolic readings. From what was said as to the mode of the production of blood pressure it becomes apparent that such short periods of rest serve to diminish the overactivity of the heart much more than they

relax the hypertonic condition of the arteries. As Boas has shown, the drop in blood-pressure obtained on lying down for a short time may persist for a considerable period after the upright position is resumed. Both these effects—the drop in pressure and its duration—are valuable aids in relieving the heart of overstrain which, as we have seen, is the main sequela of hypertension which we have to contend with if we desire to carry out prophylactic therapeutics.

Figure 223, which pictures most of the cases given in Fig. 222 and includes some others (those with a systolic pressure below 160), serves to demonstrate some of the limitations which short periods of rest have. Striking as we have noted the lessening of the arterial tension to be when measured in millimeters of mercury, it becomes very much less imposing when viewed from another angle. If we regard Fig. 223 for a moment, it becomes very apparent that arterial tension in seeking a lower level does not eliminate the entire pathologic pressure that is present. In other words, we have not succeeded in overcoming the strain upon the heart entirely, our success has only been a partial one, and if we value the results obtained by looking at Fig. 223 we are really bitterly disappointed to see what a very small fraction of the abnormal degree of tension has been done away with by our short period of rest. The enthusiasm engendered by a study of the considerable change in the blood-pressure in Fig. 222 is somewhat dampened. It becomes clear that this mode of treatment affords only partial relief from the cardiac and arterial strain, and nothing more, it is, however, extremely valuable, because it is one of the very few measures that accomplishes even this.

The results of periods of prolonged rest (several days at least) are given in Fig. 224. It is very evident that in these cases much more remarkable results are achieved than in those recorded in Figs. 222, 223, in which the recumbent position was assumed for an hour or less. The blood-pressure approximated the normal in these instances. It becomes perfectly evident that if it is urgent to relieve the heart and blood-vessels from overstrain prolonged periods of rest are much more

effective than the shorter ones. Which method of treatment is to be resorted to depends upon the condition of the heart, the degree of hypertension, and the response of the individual patient to the various forms of treatment.

It must be distinctly understood that the hypertension is not as successfully set aside in all cases as Fig. 221 would indicate. Comparing the blood-pressure observations taken day by day of 2 patients who are now in the ward you will note how in one the arterial tension was done away with while in the other no impression was made upon it by prolonged rest.

TABLE 5

ILLUSTRATING HOW THE BLOOD-PRESSURE WILL DROP WITH REST IN SOME PATIENTS, WHILE IN OTHERS IT DOES NOT

Day of rest	Blood pressure	
	Case 1	Case 2
1	238/134	205/126
2	210/118	185/110
3	218/130	190/100
4	225/135	175/100
5	211/130	165/100
10		120/80

It is, therefore, very necessary to follow the blood pressure by daily observations to determine whether or not the desired effect of relieving the circulatory strain is accomplished.

The Use of Drugs to Control Blood-pressure — The various vasodilators have had their day and have failed to furnish us with a means of permanently reducing hypertension. This is the consensus of opinion at the present time, and I do not believe that these drugs are being used extensively today. Any number of medications may be used to correct symptomatic disturbances, such as constipation, etc., but none of them has a specific therapeutic value. What is true of the vasodilators also applies to the endocrins. It may be that the future holds some medication of value in store for us, but this is a matter to be deter-

mined Chloral hydrate is one drug that has not been used frequently enough. The former idea that it is a cardiac depressant seems to be losing ground, patients, even with doses large enough to promote sleep, do not exhibit any symptoms referable to the heart. Chloral may act as a vasodilator, it certainly ameliorates nervous tension and promotes quiet. On this score it is a very valuable medication in cases of hypertension.

SUMMARY

Much has been left unsaid that might have been included in this hour. However, if certain facts stand out it is because in the practical handling of high blood-pressure a knowledge concerning them is of the utmost importance. It is worth remembering that essential hypertension is a disease that occurs commonly and is in its early stages not associated with kidney involvement, that as the increased blood-pressure persists certain secondary changes occur, these in their order of vital importance to the patient are cardiac hypertrophy, dilatation and failure, apoplexy, and nephritis and uremia, that one of the most important elements in the treatment of hypertension is the prevention of these sequelæ, that aside from symptomatic therapy there is in the majority of instances no specific effect to be expected from any form of treatment, that relief from nervous strain and rest for shorter or longer periods offers the best means of reducing the blood-pressure and relieving the strain upon the heart and arteries, for a time at least, that diet as a whole or its various constituents, proteins, fats, carbohydrates, fluids, or salt, have no direct effect upon the degree of arterial tension, indirectly the regulation of the various dietary factors so as to reduce weight, diminish the number of red blood-cells or bring about undernourishment may lower the blood-pressure, that a careful general survey of the patient will indicate what other measures should be taken in regards to the teeth, gastro-intestinal canal, genito-urinary tract, etc., which in some instances may be productive of far-reaching results. The above represents the facts concerning the treatment of essential hypertension as we possess them today, there

is much in the routine therapy of this disease that is traditional and that demands investigation before it can be successfully or conscientiously applied

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TABETIC CRISES AND ASSOCIATED GASTRIC ULCER

RECENTLY I had occasion to publish an article dealing with the subject of cerebrospinal lues associated with or complicated by chronic gastric or duodenal ulceration¹ In that paper three cases were cited and discussed to illustrate the difficulties of dissociating the symptoms of ulcer when there is concomitantly present a condition of lues involving the cerebrospinal axis The last of these cases was one of well-defined tabes clearly complicated by an ulcer, the latter giving symptoms of pain and severe hemorrhage As an operation was not performed, however, the diagnosis remained a clinical one, the visual demonstration of the ulcer remaining lacking

The following case which I wish to demonstrate is one in which there is combined both tabes and ulcer, and one in which nothing is lacking to a clear-cut presentation of the clinical picture

S A J, age forty-seven years, is engaged in the occupation of selling paints in the states of Central America He is married, has one child fourteen years old, his wife has had one miscarriage Twenty years ago he had a primary syphilitic lesion Fifteen years ago he suffered from a "paralytic stroke," at which time he received a course of antispecific treatment This was followed several years later, after the discovery of salvarsan, by a second course of treatment, this time including both salvarsan and mercury It is interesting to learn that the patient, an intelligent individual remembers that at the time of this latter course of therapy the knee reflexes were already definitely absent

The gastric symptoms date back twenty years. From that time, and up to date, he has complained of attacks of epigastric pain, occurring about one week out of every month, occasional intermissions lasting from three to six months were noted. The pains appeared three hours after eating, more marked after the heavier noonday meal, and were burning or cramp-like in character. They were relieved by bicarbonate of soda, not by food. In recent years the pains have been associated with attacks of vomiting, often very severe and prolonged, and occasionally, according to his own description, containing food residue of twenty-four hours or longer. From time to time the vomitus has been streaked with blood, no large hematemesis, however, has been observed.

The appetite is good though the patient is usually afraid to eat for fear of provoking pain. The bowels are regular, urination is normal. There has been only slight loss of weight.

The physical examination reveals a fairly well-nourished man, placid in disposition, a very matter-of-fact personality. If anything, he is hyposensitive to pain with the Libman test of pressure over the styloid process. He is well built, muscular, and shows no signs of malnutrition. The pupils of his eyes are slightly irregular, the right being larger than the left, they react slowly to light and promptly to accommodation. The thoracic examination is negative. He has well-defined tenderness on pressure over the epigastrium and slightly to the right of the median line. Otherwise the abdominal examination is negative except for complete absence of the abdominal reflexes. The knee-jerks and Achilles' tendon reflexes are completely absent. His right radial, biceps, triceps, and periosteal reflexes are active while those on the left are absent. He shows a slightly positive Romberg test. Careful tests for skin sensitivity show scattered areas of hypesthesia over the abdomen and the back. Muscular power on both sides of the body is equal. The blood pressure is 138 systolic, 85 diastolic.

It is known that in September, 1918 his blood Wassermann reaction was negative with the cholesterol antigen and four plus (---) with the alcoholic antigen. His spinal fluid

at that time showed Cells 4, globulin ++, Wassermann negative with 2 c c, Lange negative. This report was followed by another course of arsphenamin treatment. Subsequent blood Wassermann examinations have been completely negative.

At the first examination it was ascertained with but little doubt that we were dealing with a well-defined case of tabes dorsalis, the physical signs and serologic findings, as well as the history and data, all furnishing supporting links in the evidence upon which such a conclusion was justified. At first sight it seemed plausible to attribute to the tabes the attacks of pain and persistent vomiting of which the patient complained. The diagnosis of gastric crises of tabes seem to answer all the requirements, even the vomiting of small amounts of blood not being regarded as unusual in such a condition ("vomissements noires"). Thus the patient states that he would leave this country for a business trip feeling perfectly well, upon arrival in Central America he would often be taken quite suddenly with severe pain and a bout of protracted vomiting lasting for days. During these times he was unable to eat or drink and was cared for by the natives. The attacks would suddenly cease and he would continue his trip, usually without further molestation. Surely these attacks at first glance seemed quite typical of crises.

There were, however, certain facts in his history that suggested an intragastric lesion of independent origin. The patient is unable to state definitely the exact date of the onset of either the gastric symptoms or the lues, both having occurred approximately at the same time. If anything, he is inclined to the belief that the gastric symptoms were already present when the lues was contracted. On the presumption that we were dealing with an independent gastric lesion which antedated the specific infection the following data were accumulated. One year ago a fractional test-meal examination was made (Fig 225). This test revealed several points of interest. From the fasting stomach 40 c c of bile-stained secretion were obtained, an amount slightly larger than usually received, though not large enough to be of abnormal significance. The

curve of gastric acidity rose slowly to a maximum of 74 total and 56 free acidity, was maintained for one and three-quarter hours, and fell slowly to a level of 52 total acidity, at which point it was sustained. At the end of two and three-quarter hours a considerable portion of the oatmeal gruel used as a test substance was still present in the stomach. A normal range of acidity, but a type of curve indicative of a pyloric stenosis or of a pylorospasm, was clearly indicated. Blood was chemically absent from the specimens. A gastro-intestinal radio-

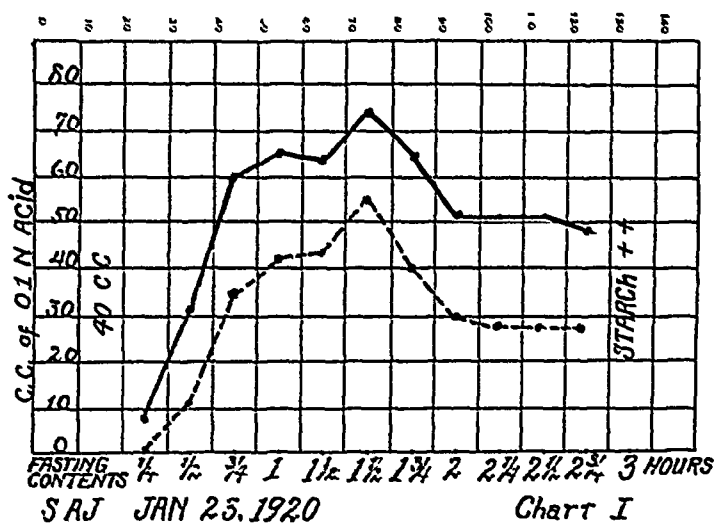


Fig 225

graph made some days later failed to show a lesion, nor was the delayed chemical motility apparent at the six-hour radiographic examination. Such incongruity between the chemical test and the x-ray examination is not very unusual, as a test of motility the former particularly a fractional test-meal, is, when properly interpreted the more reliable. In cases of intragastric lesions associated with intermittent pylorospasm one may be so fortunate on *one* occasion to be able to demonstrate by one test or another a delayed motility. At other times repeated tests may fail to show evidence of delayed motility.

During the succeeding eleven months the patient, now on a more careful diet, was fairly well, suffering only occasional attacks of pain with vomiting, at one time he had a free interval of almost six months

One month ago he presented himself again for treatment with a severe recurrence of all his symptoms. In spite of the fact that he had felt better during the last year the patient was determined to choose a radical course of treatment if such were possible. A fractional test-meal was repeated and, taken at a time when symptoms were in abeyance, showed a practically normal curve with good motility. In fact the stomach emptied in one and a half hours. Two days later a complete gastro-intestinal examination was made, both fluoroscopic and radiographic, showing the stomach to be situated normally, good tone, peristalsis somewhat increased, at times exaggerated. Food began to empty through the pylorus only after a five-minute delay. At first the emptying progressed slowly, but soon assumed a normal rate. There was some tenderness over the antrum. The duodenal cap was small, regular, and not tender. At the six-hour observation the stomach was empty and the barium column had reached the hepatic flexure. The cecum was freely movable and not tender. The twenty-four-hour observation showed no abnormality. The increased peristalsis and the tenderness over the antrum were the only findings which would indicate the presence of an ulcer at or near the pylorus.

Clinically, the diagnosis of an ulcer, therefore, rested on a history suggestive of such a lesion dating back twenty years, with recurrences and periods of intermission. The history of vomiting, often of food residue of twenty-four hours or more, suggested the pyloric lesion. Confirmation of such a fact was seen in the one fractional test-meal taken at a fortunate time and in a suggestive radiographic picture. The difficulty lay in differentiating the vomiting due to ulcer and the vomiting which might accompany a case of tabetic crises. It was practically impossible to do so. The vomiting of a food residue is unusual in tabetic crises. Delayed emptying is not usually

a part of the picture of tabes. Irregular contractions have been demonstrated by kymograph as well as roentgenographically, and an occasional case is seen where a spinal lesion causes delayed motility. Still it is recognized that the pure tabetic crisis is associated with no definite chemical disturbance of the secretory functions and no constant or clear-cut disturbances in motility. Roux has said, "Every tabetic makes his crisis with his own mucosa,"² meaning that individual variations predominate and no class picture is conceivable. The pylorospasm and the persistent attacks of food vomiting, therefore, approach that of ulcer, or, at least, that of an intragastric lesion.

It was suggested that perhaps the lues had antedated the gastric history and, therefore, that the gastric history could be accounted for on the basis of a gummatous infiltration of the organ. Syphilitic ulcer of the stomach is exceedingly rare. In this case an ulcer could not be demonstrated with the x -ray. Nor is it conceivable that a syphilitic ulcer should persist over twenty years, particularly after three courses of treatment and with a negative Wassermann for many years.

The appearance of blood in the vomitus could accompany either an ulcer or tabetic crisis. The hematemesis of tabetic crises is usually profuse and occurs at the end of a severe bout of vomiting, the so-called "black vomit," so aptly described by the French, while the bleeding due to an ulcer accompanying the tabetic process is more apt to be smaller in amount and to accompany each individual act of vomiting.

The clinical diagnosis of pyloric ulcer complicating tabes was made on the basis suggested, and the patient subjected to a laparotomy. At the operation performed by Dr. Harold Neuhof a large indurated peptic ulcer was discovered situated along the lesser curvature and the antrum and posterior wall. The base of the ulcer was distinctly felt apparently attached to the face of the pancreas by an inflammatory exudate. There was no appearance of large glands and the lesion had all the earmarks of an inflammatory rather than a new-growth process. A finger inserted in the pylorus from the duodenal side showed the pylorus markedly constricted.

A suture gastrojejunostomy (no loop) was performed without difficulty. The postoperative course was uneventful for the first five days. On the fifth day the patient vomited about 1500 cc of greenish material containing food. This vomiting persisted for the next seven days in spite of daily or twice daily lavages. A fluoroscopic examination at this time showed dilated duodenum and consequent regurgitation from the duodenum into the stomach through the pylorus. Little if anything was passing the stoma. This was rather startling, as the stoma was large. There was no rise of temperature to evidence any surgical complication. After seven days the vomiting ceased. The food was retained and the usual postoperative course pursued. It is difficult to understand just what happened at this time, nor is it possible definitely to assert whether we were dealing with some mechanical defect of the operative technic or whether we were still in the presence of tabetic crises.

The occurrence of ulcer as a complication of tabes is one of the frequency of which has yet to be determined. The French literature contains several articles on the subject, most of them being unrelated case histories with here and there an attempt to unite similar cases and draw up a clinical picture. Recently Klippel and Weil³ and also Lehmann⁴ have attempted to disengage the organic causes for hematemesis in the course of gastric crises from those in which the symptoms are due alone to the neurologic lesion. In the attempt to classify the cases reported in the earlier literature one meets with two objections: one, the absence of the Wassermann reaction, or other specific reactions for syphilis in the earlier cases, and two, the absence of roentgenologic data previous to quite recent years.

The approach to the subject has been through the discussion of the frequency with which hematemesis has accompanied the vomiting of tabetic crises. Hematemesis under these circumstances was first discussed by Charcot⁵ and again by Vulpian.⁶ In the course of years about 35 cases have appeared in the literature. Considering the frequency of tabes and the not infrequent occurrence of gastric crises in the early stage of tabes, 35 cases of hematemesis are not many.

The cases are classified by Lehmann⁴ into One, *true hematemesis accompanying tabes*. These are the cases in which vomiting of blood is an incident or an accident of violent vomiting in the crises. The vomiting of blood under these circumstances is rarely profuse, occurs at the end of the crisis, and only after repeated and protracted bouts of wrenching and vomiting. There are about 15 such cases reported in the literature. Such crises are not infrequently accompanied by the appearance of a large roseola, herpetic or purpuric eruption. In the cases of true hematemesis numerous attempts have been made to explain the phenomenon. Most of them emphasize the so-called "suffisiones hemorrhagiques" of Strauss,⁷ who attributed the hemorrhage to the congestion of the mucosa of the stomach and the violence of the vomiting acts.

Two, a group of cases which includes those in which there is a factor other than the tabes to cause the hematemesis (*false hematemesis of crises*). Such factors may be trauma applied to the abdomen or biliary calculi complicating the crises, but is mainly constituted by cases in which a peptic ulcer or a carcinoma of the stomach occurs with the neurologic phenomena. There are at least 9 true cases of ulcer under these circumstances, practically all of them confirmed at autopsy or operation. One of them is described in American literature by Hitchcock⁸ and was a perforating ulcer of the posterior surface near the lesser curvature. I do not believe that anyone is able to say how many of the other cases of so-called true hematemesis were really cases in which ulcer occurred. In the group of cases wherein an organic lesion complicates the crises the hematemesis is more profound and serious and precedes (often as a melena) or appears irregularly in the course of the crises. The blood may vary in color from wine or bright red to black or coffee-ground color, and varies in amount from 150 to 400 or 500 c c. Exsanguination may occur.

In the ulcer cases erosion of an artery has been demonstrated. Since the publication of my former paper on this subject I have had two oral communications from fellow practitioners in the West, one of a perforated ulcer in the midst

of a tabetic crisis attack, and the other profound melena due to ulcer. It may be argued that the incidence of ulcer in tabes is no greater nor less than would be found in any other group of cases. The statistics on the occurrence of gastric ulcer in the civil population vary, Berthold quoting 2.7 per cent, Nolte 1.23 per cent and Orth as high as 5 per cent.⁹ In the group of cases of tabes with gastric symptoms it is likely that the incidence of ulcer is higher. Certainly in the published cases from 25 to 33 per cent of those who have hematemesis are proved ulcers. Presumably the ulcer is simple benign and not a syphilitic ulcer. Thus in the case of Ewald,¹⁰ published in 1910, the ulcer was proved to be a simple ulcer, not specific. The necropsy material investigated by Chian¹¹ showed that in syphilitics only 2 out of 243 autopsied cases showed gastric syphilis. There was only 1 case in which an ulcer occurred and that was benign and non-syphilitic. Thus we note that ulcer occurring in syphilis may well be the usual non-specific type of indurated ulcer, while presumably patients suffering from ulcer who in later years become infected with syphilis still bear their simple ulcers which run their courses uninfluenced by the luetic infection. While discussing the subject of ulcer and false crises one may mention a type of ulcer uncomplicated by any nerve lesion, but whose course is characterized by attacks of violent pain and protracted vomiting, such attacks occurring once or twice a year, lasting a few days, and leaving free intervals of many months between the exacerbations. Such cases have recently been again described under the title of "Gastric Ulcer with Incoercible Vomiting" by Le Noir, Richet, and Jacquelin,¹² and also by Savignac and Alivisatos.¹³ In some of their cases a kidney or liver complicating factor was suggested. However, I have seen and treated such a case for years, being required to administer morphin repeatedly for the violence of the attacks which came on suddenly and ended rather suddenly. I anticipated either gall-stones or tabetic crises, though the specific serologic reactions were missing. A sudden perforation of a duodenal ulcer revealed the correct diagnosis. The exacerbations of the ulcer in such a case assume the typical

form of violent tabetic crises. The latter is seriously to be considered in the differential diagnosis of such a condition.

The third set of cases classified by Lehmann⁴ includes a group of "Pseudotabes Polyneurotique," by which is meant and described gastric ulcer with symptoms of peripheral polyneuritis, simulating, in clinical respects, tabes. In these cases the Wassermann reaction is negative and the autopsy fails to reveal the degeneration of the posterior and posterolateral group columns characteristic and essential to the diagnosis of true tabes. This is a small group comprising only 6 cases. In all of them a large indurated ulcer was demonstrated, and in many of them degeneration of peripheral nerves, such as the sciatic, has been demonstrated. I have never seen clinically nor have I ever seen described in the American literature cases of this kind. The picture of pseudotabes, that is, a sensory and ataxic disturbance referred to the periphery and not due to a specific luetic infection, we associate in our mind with pernicious anemia or with arsenic- or lead-poisoning, Hodgkin's disease, etc. It is hard to understand why such a process should accompany a chronic indurated gastric ulcer. The cases, however, in the French literature have been carefully studied, degeneration has been demonstrated in the sciatic and other peripheral nerves, but not in the lumbar or dorsolumbar levels of a cord. Such a clinical condition could easily simulate true tabes or tabes complicated by ulcer.

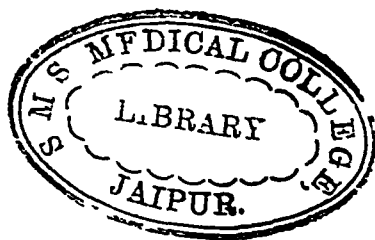
In the clinical differentiation there must also be taken into account a form of tabetic dyspepsia which has been described by Roux,² and which is not infrequently seen. Such a dyspepsia, often due to improper diet and often due to the use of drugs, is characterized by pain after meals, eructations, abdominal distention. Such a picture may precede the crises, or may occur independently of crises, and may even be intermingled with attacks similar to gastric crises. It is often difficult to differentiate and to interpret these gastric symptoms. In many of the cases which one sees in every-day practice one has the early signs of locomotor ataxia, and one has indefinite or indeterminate gastric symptoms with or without vomiting.

In these cases one may not be able at all times to differentiate the symptoms of an independent gastric lesion from those of a pretabetic dyspepsia, or from those of tabetic crises. Above all, it is essential to remember at all times that ulcer may occur independently of or as a complication of tabes.

It would need all of our best laboratory methods, clinical, roentgenographic, as well as the closest application of clinical knowledge in physical diagnosis, properly to classify the symptoms in such a case.

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CONTRIBUTION BY DR WARFIELD T LONGCOPE

NEW YORK CITY

EPIDEMIC JAUNDICE WITH SPECIAL REFERENCE TO MILD FORM OCCURRING IN THE UNITED STATES

THE recent occurrence of cases of jaundice appearing in groups or in families in different parts of the United States has created considerable interest in such localities. Our knowledge of these milder forms of epidemic jaundice is still very incomplete, and at the present time the relationship of such cases to the true infectious jaundice caused by the *Spirochæta icterohæmorrhagiæ* is unknown. Since it is highly desirable that attention should be directed to these mild cases of jaundice occurring in families and in certain communities in order that detailed reports may be made upon selected groups of cases, I am presenting two instances which it seemed to me belong to this group.

CASE I.—The first patient, a boy aged nine, was seen on November 3, 1921 by reason of the fact that he had had during the summer occasional attacks of some form of gastro-intestinal disturbance and had lost weight. The family history was such that the father as a boy had had an attack of what he believed to be catarrhal jaundice. The patient when a baby had had a severe gastro-intestinal disturbance which was attributed to the use of and oatmeal in his diet. He had had measles at the age of one and a half, whooping-cough one year and a half ago, and had been removed in the spring of 1920, after which he had had a temporary enlargement of the spleen.

He has been subject to occasional colds. Following the tonsillitis he had been quite well until last spring, when he had an attack of pain in the epigastrium, with slight nausea and constipation, without fever, headache, or rash. This attack lasted for one or two days. In the summer he had had three such attacks, but had vomited in only one of them. His appetite had been poor during the summer and he had lost 5 pounds in weight. In August, 1921 he was vaccinated with vaccine virus and experienced a rather severe "take." During the latter part of the summer he had had several furuncles over his body.

For some weeks he had been quite well, when, on October 30th, he seemed to feel poorly, complained of slight pain in the epigastrium, and was constipated. His appetite diminished. His temperature was 99° to 100° F. His pulse was slow. On the morning of November 3d he vomited.

Examination on November 3d showed a rather pale, languid boy who evidently when well was quite bright and intelligent, complaining of pain in the epigastrium, which, however, was not very severe. His face was not flushed. The temperature was 99.2° F, the mucous membranes appeared slightly pale. The submaxillary, cervical, and inguinal lymph-nodes were just palpable. The epitrochlear and axillary nodes could not be felt. The skin was smooth and delicate, and there were no eruptions. There were scars of furuncles on the abdomen and back. The lungs were clear to auscultation and percussion. The maximum impulse of the heart was readily localized in the fourth space inside the midclavicular line. The heart was not enlarged. The sounds were clear, regular, and loud. There were no murmurs. The pulse was regular, 90 to the minute.

The abdomen showed slight fulness in the epigastrium, where there was a moderate degree of tenderness. Here the abdominal wall was slightly more tense than elsewhere. There was no rigidity. The lower quadrants of the abdomen were soft and there was no tenderness. In the right costovertebral angle there was very slight tenderness. The edge of the liver was readily palpable in the midclavicular line 3 cm below the costal margin, and there seemed to be some tenderness over it.

a healthy child, but had had chickenpox and whooping-cough. In December, 1920 her tonsils had been removed, after which she had fever reaching 103° F, with an infection of the facial sinuses. These were treated without puncture. During the summer she had been quite well and had gained 20 pounds in weight. Following the coryza there was some cough and mucous nasal discharge. In view of the history of sinus infection it seemed desirable that the sinuses should be carefully examined at this time, and the patient was, therefore, referred to Dr Coakley, who found a chronic infection of practically all of the facial sinuses. Treatment was immediately begun to relieve this infection.

On December 3d, thirty days after the onset of her brother's illness, the patient complained of feeling somewhat nauseated and generally lackadaisical. There was anorexia, but no fever or abdominal pain. On December 4th she vomited and practically refused all food. On December 5th these symptoms continued and the pulse in the dorsal position was said to be slow and irregular. On December 6th the patient looked rather pale, slightly prostrated, and continued to refuse food, complaining of a little pain in the upper part of the abdomen. She was nauseated and preferred resting on a couch to playing about. There was no tenderness over the facial sinuses. The temperature was 98.2° F. The lungs were normal. The maximum cardiac impulse was in the fifth space inside the midclavicular line, there was no increase in cardiac dullness, no heave, and no thrill. The heart sounds were loud. There were no murmurs. The pulse was 72 and distinctly irregular, disclosing the sinus type of irregularity. There was a distinct acceleration on inspiration and marked slowing on expiration, the blood-pressure was 110/70. There was no stiffness of the neck, Kernig sign, or Brudzinski. The deep reflexes were normal.

In the afternoon of December 7th it was noted that the patient was distinctly jaundiced. On examination the skin and scleræ were a pale lemon yellow. The abdomen was generally soft and not distended. There was some tenderness on deep pressure in the epigastrium. The liver was readily palpable.

On the evening of the 5th, six days after the onset of the acute illness, there was noted a slight ictteroid tinge to the conjunctivæ and to the skin. On November 6th the boy had improved very markedly. He was taking milk, and though there was still slight nausea and some pain in the epigastrium, it was not nearly so marked as it had been. He was definitely jaundiced. The scleræ had a lemon-yellow tint. The liver remained about the same size. The tenderness over it had decreased. The urine was dark and greenish in color. On the 7th jaundice had increased, but the nausea and epigastric pain had diminished. The urine was amber, clear, 1010, acid, very faint trace of albumin, no sugar, microscopically showed an occasional mucous thread, acetone and diacetic acid were present. The stools were rather light in color, but were not actually clay colored. On November 8th the urine was amber, clear, 1015, acid, very faint trace of albumin, no sugar, microscopically showed occasional white blood-cells, acetone, diacetic acid, and bile were present. By November 9th the jaundice had diminished, his appetite had returned, and he was rapidly improving. The stool was pasty, light grayish-yellow, small amount of residue with some mucus, no blood, ova, or parasites. By November 11th the urine was free from bile, lemon yellow, cloudy, 1018, alkaline, showed no albumin or sugar, microscopically there were occasional white blood-cells and mucous threads, acetone and diacetic acid were still present, though on the 12th the skin and conjunctivæ were still slightly yellow. The liver was readily palpable 3 cm below the costal margin. Convalescence was rapid and he was soon up and about and back at school.

On November 26th he had completely recovered, though there persisted for some weeks a faint yellow tinge to the conjunctivæ. Bile had been absent from the urine since November 10th. His weight was 67½ pounds. The liver was still palpable, but it was not tender. The spleen could be felt with ease on deep breathing coming just below the costal margin.

CASE II—During this boy's illness his sister, aged ten, developed a rhinitis and acute coryza, and for this reason was examined and found otherwise normal. She had always been

Hokū, Ito, and Wani¹ showed conclusively that *Spirochæta icterohæmorrhagiæ* may occur in the organs of rats, since they found nearly 30 per cent of all the rats examined in certain regions of Japan to be infected Stokes, Ryle and Tytler,² and Martin and Pettit³ were able to demonstrate this type of spirochete in rats captured on the western front during the war

The occurrence of epidemics of jaundice in the United States has stimulated some interest in the study of the etiology of the condition in this country The experiments of Noguchi⁴ have shown without question that strains of *Spirochæta icterohæmorrhagiæ*, which are indistinguishable from those coming from Japan and Belgium, occur in wild rats collected from different parts of this country Noguchi gathered together a large number of wild rats from different regions and removed their kidneys for the purpose of ascertaining whether or not these organs contained spirochetes which would produce the typical experimental lesions characteristic of infectious jaundice By inoculating the emulsion made of kidneys from 41 wild rats into 58 guinea-pigs he was able to produce in three groups of guinea-pigs the typical icterohæmorrhagic spirochetosis, in all respects identical with the lesions observed in the guinea-pigs which died from inoculations of the Japanese and Belgian strains It is, therefore, evident that the organism which is capable of inciting infectious jaundice is present in the United States and occurs as an infection among rats It is, accordingly, important to know whether any of these epidemics of jaundice are produced by this specific organism

There are a few published reports which have bearing upon the etiology of the cases of epidemic jaundice in this country Symmers⁵ has published a description of 16 cases of acute jaundice which occurred at Bellevue Hospital in New York City All of these cases were extremely grave and there were 9 fatalities One group was characterized by the presence of bronchitis,

¹ Jour Exp Med, 1916, xxv, 485

² Jour Roy Army Med Corps, 1916, xlvii, 286

³ Cont Rend Soc Biol, 1917, lxxx, 10

⁴ Jour Exp Med, 1917, xlv, 755

⁵ Jour Amer Med Assoc, 1920, lxxv, 1155

epidemics of jaundice occurring at intervals in different parts of the United States, and in this older literature these epidemics are usually referred to as instances of Weil's disease. In 1886 Weil¹ described a form of jaundice occurring in epidemic form which was accompanied by fever and enlargement of the spleen, evidence of nephritis, and which in a fair proportion of cases was fatal. A disease which corresponded to this description was noted subsequently from time to time in various countries and was common in Japan.

In 1914 Inada and Ido, with their associates,² succeeded in transmitting to guinea-pigs the typical experimental disease which in these animals was accompanied by jaundice, hemorrhages, and albuminuria. The transmission was accomplished by inoculating guinea-pigs with the blood of patients suffering with the Japanese form of infectious jaundice. They further discovered in the blood and various organs of the inoculated animals, as well as in the blood and organs of human cases, a new spirochete which they designated *Spirochæta ictero-hæmorrhagiæ*. This organism could be cultivated upon appropriate media, and when inoculated into guinea-pigs gave rise to the same disease that was produced by the inoculation of blood of human cases of Weil's disease. Since the publication of their original work this type of infectious jaundice has been identified by the discovery of the specific organism in various parts of the world, and occurred as one of the serious, though not very common, infections among the English, French, and Italian troops on the western front during the war. An excellent description of the disease is given by Dawson and Hume.³

Further experimental work upon the etiology of infectious jaundice and the transmission of the disease showed that the spirochetes were eliminated in large numbers in the urine, particularly during the later stages of the disease and in convalescence. It is, therefore, discharged over long periods of time from the urinary tract. The observations of Inada, Ido,

¹ Deut Arch Klin Med, 1886, xxxix, 209

² Jour Exp Med, 1916, xxiii, 377

³ Quart Jour Med 1917, v, 90

"Epidemic Jaundice Suspected in the State —According to a report of the state department of health the state health officers are actively investigating what is suspected to be epidemic infectious jaundice, a disease hitherto rarely reported in the United States Following recent descriptions of several groups of suspicious cases in Madison, Oswego, and St Lawrence counties State Health Commissioner Hermann M Biggs has directed that the full resources of the department be employed in a state-wide investigation through the sanitary supervisors and the laboratory staff "

At the present time there is no evidence apparently to show that the epidemic jaundice occurring in this country at the present time is caused by *Spirochæta icterohæmorrhagæ* It seems probable, indeed, that other organisms may produce a form of jaundice that may occur in epidemics, for Hurst found that the jaundice which occurred in Salonika among British troops and which was first supposed to be due to the *Spirochæta hæmorrhagæ* was, in fact, caused by an infection with paratyphoid bacilli

Since so little has been published upon what has appeared to be epidemics of mild jaundice in this country it is desirable to draw your attention to the fact that such exist and urge those who have an opportunity to do so to study with great care the clinical features of the disease, the epidemiology, and, when possible, the etiology.

lassitude, occasionally vomiting and diarrhea, intense jaundice, epistaxis, hematuria, melena, and hemorrhagic vesicles. There was frequently stupor or delirium. Fever was present in some of the patients, but in others it was absent. The stools were clay colored. The leukocytes varied from 20,000 to 24,000. The urine showed albumin, bile, and casts. At autopsy the icterus was extreme. There was cloudy swelling of the kidneys, the liver frequently presented the appearance which is observed in acute yellow atrophy. In the second group the course was extremely rapid, with jaundice, wild delirium, and rapid death. In this group autopsy frequently disclosed deep areas of necrosis in the gastro-intestinal tract. Eight of these cases were examined during life, with special reference to the presence of spirochetæ. Both the blood and urine were examined microscopically, and, moreover, injected into guinea-pigs. The results were all negative. In 3 of the fatal cases the liver was searched for spirochetæ, but none were found. Through the kindness of Dr Noguchi it was possible to examine the excreta of these 2 cases of mild jaundice to determine whether they contained during the disease or during the convalescence *Spirochetæ icterohæmorrhagæ*. Results from guinea-pig inoculations were entirely negative, and no evidence of the presence of this organism could be discovered by Dr Noguchi in either case.

The type of disease which is described by Symmers is extremely severe, but in many of the epidemics, descriptions of which come to one usually by word of mouth, the course of the disease in children is very mild. Stokes, Ruddeman, and Lemon¹ refer to a moderately mild epidemic type which two years ago was common in Minnesota, and in the autumn of 1921 I happened to see a number of such cases with slight fever and jaundice which occurred at that time in New Haven, Conn. Indeed, reports of cases of jaundice occurring as house or town epidemics are coming from various parts of the state, and it is of interest to quote a note in a recent number of the Journal of the American Medical Association which gives some idea of the prevalence of this disease and the interest that it is creating

¹ Arch Int Med, 1920, xxvi, 521

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CLINICAL-PATHOLOGIC CONFERENCE OF
DRS ALBERT R LAMB AND
WILLIAM C VON GLAHN

PRESBYTERIAN HOSPITAL

STAPHYLOCOCCUS AUREUS ENDOCARDITIS

WE have 3 cases for discussion today, and we trust that a consideration of some points in connection with these cases will serve to fix in your minds a certain type of endocarditis

In the past we have tried to formulate for you the clinical and pathologic picture of non-hemolytic streptococcus endocarditis and in so doing have pointed out the fact that the endocardium may be affected by many, if not all, of the known bacteria. Such an involvement constitutes an endocarditis, and we have spoken of it as a bacterial endocarditis in contradistinction to rheumatic endocarditis, arteriosclerotic endocarditis, and the forms following such cachectic conditions as tuberculosis, carcinoma, nephritis, etc. Limiting ourselves to the bacterial endocarditides, we have urged you to give up such partially descriptive terms as malignant, septic, infectious, vegetative, ulcerative, etc., in favor of the name of the offending organism. This is possible because the diagnosis practically depends upon culturing the organism from the blood. Such an etiologic classification clears the air for a better understanding of the various groups of endocarditis and prevents jumbling them all together into one big group. From this mixed crowd of the endocarditides the non-hemolytic streptococcus form has been separated into such a clear-cut entity that in most cases it is quite possible to make a positive diagnosis without the aid of blood-cultures. While it may be impossible to evolve equally clear-cut pictures for the other bacterial cases, every

effort should be made along that line. And we feel reasonably convinced that if we begin to study each group by itself many important facts are bound to be correlated with their respective groups.

Today we wish to consider the clinical and pathologic pictures caused by infection of the endocardium by the *Staphylococcus aureus*. And when we remember that it was less than twenty years ago that a rather heated discussion took place at a meeting of the New York Pathological Society as to whether a *Staphylococcus aureus* found in blood-cultures had any real significance or was merely a contamination, and when we find how little literature there is on the subject, it is not unreasonable to hope for a broadening of the picture through future study, nor unprofitable for you to have your attention directed to it.

We have not time today to discuss these cases from the aspect of *Staphylococcus aureus* infections in general, interesting as that would be. We shall present their case records to you in full, but shall limit the discussion to the cardiac features. We ask you to remember that all 3 of these patients were desperately sick during the period of hospital observation and that, in consequence, there are numerous omissions in their records.

CASE I

(J H History 52,010) A young schoolboy, aged thirteen, entered the hospital November 16th, with a history of having fallen upon his right knee five days previously. Since then it had been so painful that he had had difficulty in getting about. On the day before admission he felt chilly and sick and went to bed.

Further questioning developed the fact that in 1919 he had had a furuncle on his forehead and in April, 1921, one on his nose. In addition, he had had a "sore" on the dorsum of his right foot for two weeks preceding his injury, and from this "sore" pus had been expressed on the day before coming to the hospital.

Physical Examination — Temperature, 103° F, pulse, 88,

respirations, 26 A rather pale and poorly nourished young boy with an acneform eruption upon his face He had the configuration which, for want of a better term, we call the "status" type The teeth showed some decay The tonsils were small and not inflamed Lungs clear Heart normal Abdomen negative The right knee was larger than the left and showed two pus blisters on the inner aspect surrounded by a reddish area, and a scab on the outer side There was tenderness over the inner aspect of the knee and a sense of induration A blood count showed 16,600 leukocytes with 91 per cent polymorphonuclears An exploratory incision over the tender, indurated area did not reveal any pus, and on the following day the tibia was explored and an osteomyelitis extending the length of the bone was drained The blood-culture taken on admission was now definitely reported to contain a hemolytic *Staphylococcus aureus*, and cultures from the osteomyelitis showed the same organism

Course—November 18th Flushed and very ill Temperature, 104° F, pulse, 118 Lungs negative anteriorly Abdomen tense, but not tender, liver and spleen not felt

	Right	Space	Left
Heart	2 cm	3	9 cm
	2 cm	4	10 5 cm

Action rapid, but regular There is a crescendo quality to the first sound, which is forcible There is a systolic murmur over the pulmonic area and the pulmonic second sound is accentuated W B C 17,600, with 93 per cent polys

November 19th Somewhat improved Alert No petechiæ Heart sounds of fair quality At the apex there is a systolic thrill and a rumbling, rough, first sound No friction-rub Lungs clear anteriorly Posteriorly near angle of right scapula there are a few râles and high-pitched nasal voice Abdomen negative and spleen not felt There is some pain and tenderness over the region of the thyroid gland

November 20th About the same Throat sore, some cough W B C 6800, with 68 per cent polys

November 21st Wound shows very little discharge There is evidence of an abscess over or within the thyroid W B C 9800 Polys 88 per cent There are still indefinite signs of pneumonia at the angle of the right scapula Heart unchanged Blood-culture shows hemolytic *Staphylococcus aureus* in both flasks

November 22d Much worse Temperature, 106° F, pulse, 150 W B C 26,400, polys 92 per cent Failed gradually and died that day Urine examinations were negative, but no cultures were made

During his course the temperature was never below 102° F and was irregular between that point and 106° F, while the pulse was between 100 and 150

Autopsy 9176 The body is that of a rather well-developed boy, 162 cm in length There are no cutaneous petechiæ seen The hips are rather narrow The line of the pubic hair is straight. There is no hair in the axillæ, and only a small amount over the thighs and legs There is no superficial glandular enlargement There is a large open wound in the inner side of the right leg, 29 cm in length, extending down to the mesial surface of the tibia from one epiphyseal line to the other The cortex of the bone has been chiseled away on this surface and the cavity of the bone is filled with soft, semisolid, purulent material in the upper part, in the lower part there are reddish-black clots The margins of the wound in the soft parts are covered with a purulent exudate The right knee-joint contains a slight excess of clear fluid The internal and external saphenous veins, also the femoral and tibial veins, are quite free of thrombi The abdominal cavity is negative In the mesentery are found several calcified lymph-glands Each pleural cavity contains a slight excess of turbid fluid The pericardial cavity is negative

The heart weighs 340 grams The epicardium is everywhere smooth and glistening The chambers contain post-mortem clot and are otherwise negative The tricuspid ring measures 12.5 cm in circumference The left leaflet of the valve is quite thin and delicate throughout On the right half of the posterior or septal leaflet there is a delicate fibrinous

exudate along the line of closure. The portion of the valve involved measures less than 1 cm in length and only a few millimeters in width. The exudate is quite adherent, and the valve surface beneath it is roughened and slightly ulcerated. The left half of the right leaflet, also along the line of closure and extending downward to the free border of the valve, is in part covered by a delicate fibrinous exudate, but the changes

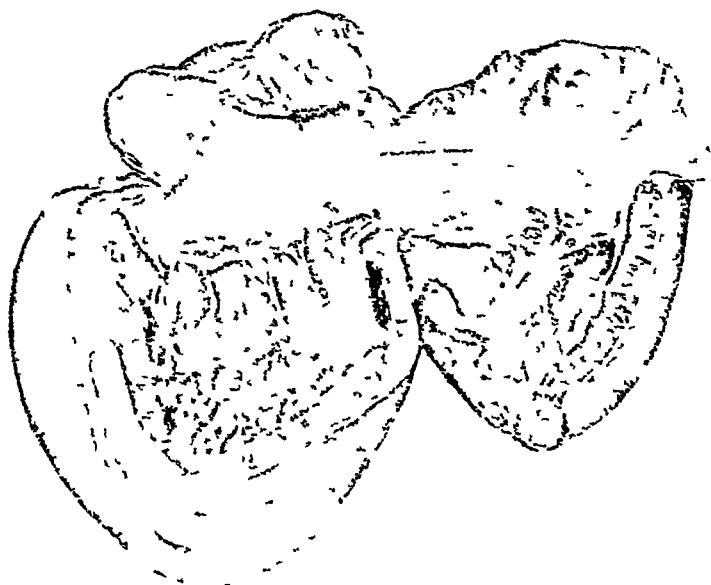


Fig 187—Case 1 Staphylococcus aureus endocarditis tricuspid valve

in this leaflet are more advanced than in the one just described. The valve in this part appears slightly thickened, distinctly yellowish and opaque, and about this area is a narrow zone of fresh hemorrhage. The aortic leaflet of the mitral valve is slightly thickened, and there are several small, translucent nodules close to the margin of the valve. The pulmonic and aortic valves are negative. The myocardium shows no changes (Fig 187).

The *right lung* weighs 250 grams. There is a delicate fibrinous exudate on the posterior surface of the lower lobe, and also on the lateral surface of the middle lobe. There are numerous subpleural petechiæ seen everywhere over the lower lobe. In the middle lobe is a firm area, which on section is found to be dark red in color. It reaches to the pleura and is quite obviously an infarct. The lower lobe shows numerous areas of bronchopneumonia.

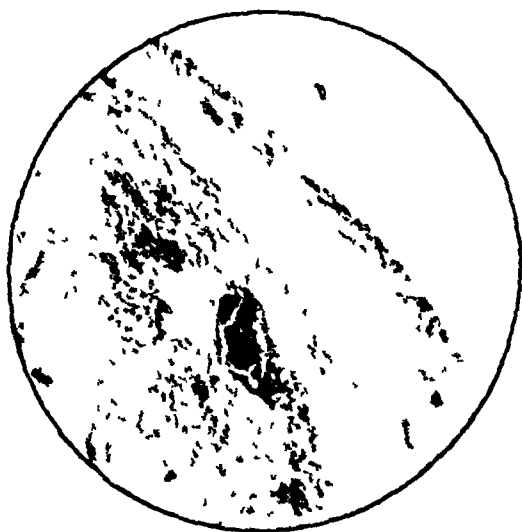


Fig 188—Case 1. *Staphylococcus aureus* endocarditis tricuspid valve. Masses of bacteria in depths of valve and in exudate upon the surface.

The *left lung* resembles the right in its external appearance. In the lower lobe there are several characteristic infarcts, in one of which there are seen small abscesses.

The *spleen* weighs 230 grams and is rather soft. The pulp is soft, reddish-gray, and opaque.

The *thyroid* is swollen. On section it is found to contain numerous pockets of yellow pus of varying size.

The other organs show nothing abnormal.

Histologically, the sections of chief interest are those of the tricuspid valve, the lungs and the thyroid.

In the section of the tricuspid valve the endocardial surfaces are covered with fibrin in which are numerous clumps of cocci. Also in the depths of the valve are found masses of bacteria, similar to those on the surface, and there is necrosis of the tissue surrounding them (Fig 188). These bacteria with the Gram stain are found to be Gram-positive, and are in large clumps, resembling staphylococci.

The sections of the lungs show quite characteristic infarcts, in some of which there is beginning abscess formation, and in others there are frank abscesses. The vessels in the infarcted portion often contain large clumps of cocci. The walls of these vessels are frequently necrotic. In other vessels there are seen emboli which are also infected. In addition to these changes there are areas of lobular pneumonia.

The section of the thyroid shows an acute diffuse suppurative process, with extensive necrosis of the glandular tissue.

The spleen shows the changes characteristic of acute splenic tumor.

In the kidney there is found a small abscess in the cortex.

In the bronchial gland there are several small caseous tubercles.

The anatomic diagnosis is: Acute osteomyelitis, right tibia, *Staphylococcus aureus* septicemia, with abscesses in the kidney and thyroid, acute splenic tumor, embolic infarcts in the lungs, lobular pneumonia, confluent, acute fibrinous pleurisy, acute endocarditis—tricuspid valve (*Staphylococcus aureus*), tuberculous lymphadenitis, bronchial gland, calcification of mesenteric glands.

CASE II

(H W History 52,083) A boy, age thirteen, returned from school six days before admission to the hospital, limping slightly and complaining of pain in the left knee-cap. There had been no known injury to his knee. Several days before the onset he had had a slight cold and cough. On the day after onset the pain was worse and he went to bed. From that time until admission, November 23d, he had severe pain, anorexia, vomiting, fever, prostration, and at times delirium.

Physical Examination—Temperature, 103.8° F, pulse, 132 respirations, 42. A frail, stuporous, slightly cyanotic boy who was a little irrational and seriously ill. Tongue dry and coated. Pharynx congested. Cervical glands just palpable. Some dulness at base of right lung posteriorly with fine râles at both bases. Heart overactive, but regular. There is a soft systolic murmur at the apex. Abdomen negative. Spleen not felt. No petechiæ. Entire left leg from below knee to the hip swollen, hot, and tender. W B C 21,200, polys 87 per cent. The urine showed a faint trace of albumin and a few leukocytes and red blood-cells. No sugar. A diagnosis of osteomyelitis of the femur was made, and bearing in mind the previous case, the following additional facts in his history were obtained. Last spring and summer he had had several boils, but none lately. One month before onset an abscess in his ear had been opened. From the description, this was a furuncle in the canal.

Operation was performed immediately. Osteomyelitis of the femur was found and drained. Cultures from this as well as from the blood showed a hemolytic *Staphylococcus aureus*.

Course.—November 24th. A little better. Abdomen tense, but not tender. There is a friction-rub over the left border of the precordial region, affected by respiration. W B C 15,600, polys 72 per cent.

November 25th. Rapid, grunting respiration, with marked cyanosis. Heart action rapid, but regular. There is a systolic murmur at the apex and a friction-rub which seems to be pleuropericardial in nature. Lungs clear anteriorly. Posteriorly there is dulness, with patchy bronchial voice and breathing over the left lower lobe, and dulness with a friction-rub over the lower half of the right lower lobe. W B C 20,200, polys 89 per cent. In the evening temperature 106° F, pulse 130, respirations 60. Marked dyspnea and slight cyanosis. No petechiæ or skin eruptions. No signs of meningeal irritation. Ear drums normal.

November 26th. Slightly better. W B C 16,000, polys 93 per cent. Blood-culture showed a hemolytic *Staphylococcus aureus*. Sweats profusely.

November 27th Grew gradually worse and died during the night

Throughout the period in the hospital the temperature varied between 102° and 106° F

Autopsy 9177 The second case resembles in many respects the case just described The body is that of a boy, 142 cm in length There are no secondary sex characteristics developed The external examination of the body is negative except the left thigh Here on the mesial surface is a widely gaping wound, extending 17 cm upward from the knee The surfaces of the wound are covered with granulation tissue and purulent exudate The incision extends down to the bone, and the cortex has been removed from the mesial surface of the femur, beginning in the middle third and extending down to the condyle The marrow cavity is widely open, there are some granulations in it, and in the lower end a small amount of clotted blood In addition to this, the periosteum has been separated from the bone on the posterior surface of the lower third, and there is a second incision on the lateral surface of the thigh, which communicates directly with the one just described The knee-joint is negative except for a slight increase in the amount of fluid contained in it The muscles of the thigh along the incision are edematous and contain numerous small pockets of pus The femoral vein in the lower half of the thigh is rather distended and firm, and when opened is found to contain a large thrombus which had undergone puriform softening The upper half of the vein and the external iliac vein on this side were free of thrombi

The abdominal cavity is negative The pericardial cavity does not contain an excess of fluid

The epicardium of the *heart* is smooth and glistening On the anterior surface at the apex there is in the fat a small abscess filled with yellow pus, and on the posterior surface of the right ventricle in the fat, just below the auriculoventricular groove, there is a second slightly larger abscess The heart weighs 170 grams Attached to the septal or posterior leaflet of the tricuspid valve is a conical, grayish-red thrombus mass, 3 cm in length and about 1 cm in diameter (Fig 189) The valve

leaflet has been destroyed below this thrombus, and posterior to the leaflet there is a large, soft, white, opaque, friable mass filling the space between the leaflet and the septum. Below the aortic leaflet, in the septum membranaceum, there is a perforation about 0.5 cm in greatest diameter. The edges of this opening are covered with fibrin and a probe passes through

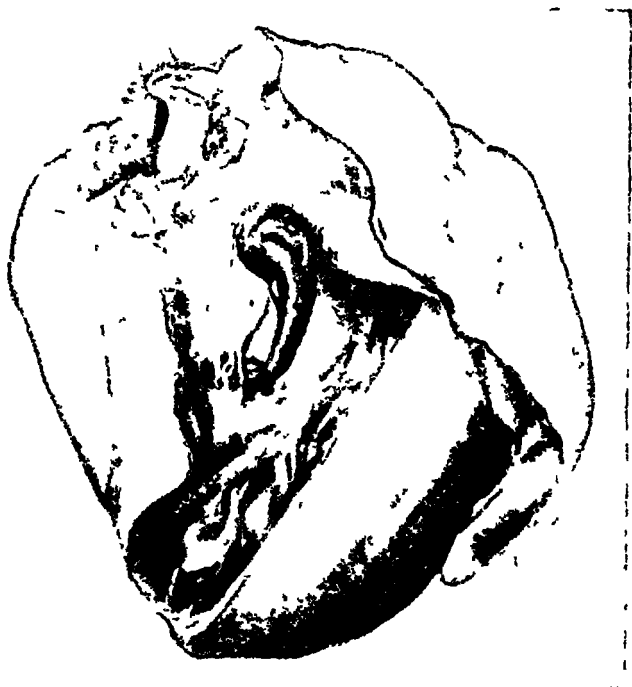


Fig. 189—Case 2. *Staphylococcus aureus* endocarditis, tricuspid valve.

it into the thrombotic mass lying posterior to the tricuspid valve (Fig. 190). In the myocardium of the left ventricle there are two small abscesses. The heart otherwise is negative.

The right pleural cavity does not contain any fluid. The right lung weighs 430 grams. The entire surface of the lower lobe is covered with a thick, fibrinopurulent exudate. The surfaces of the upper and middle lobes are partly covered with

a similar exudate Projecting above the surface of all parts of the lung are elevated rounded knobs, the centers of which are yellowish and softened These, on section, are found to be abscesses which are filled with yellow pus Also in other parts of the lung there are irregular areas of consolidation, in the centers of which are beginning abscesses, and beneath the pleura one sees somewhat wedge-shaped, dark red areas of consolidation which appear to be infarcts

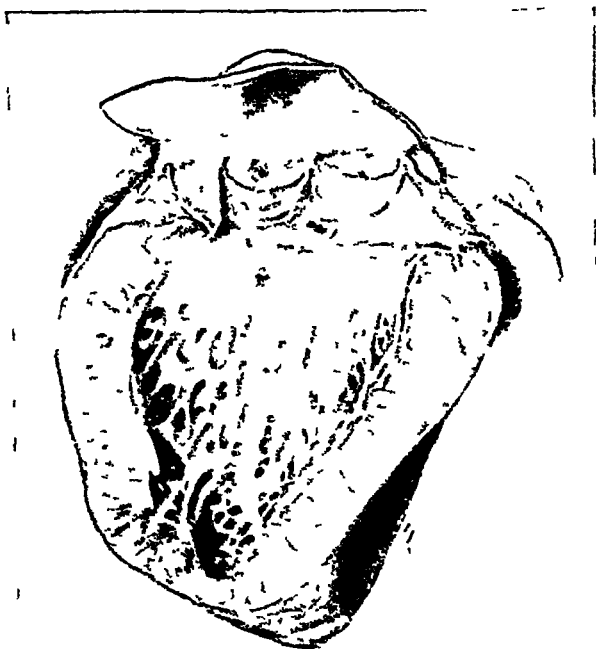


Fig 190—Case 2 Perforation of interventricular septum (Staphylococcus aureus endocarditis tricuspid valve)

The *left lung* is similar to the right

The *spleen* weighs 200 grams It is moderately soft The pulp is pale grayish-red, rather opaque The malpighian bodies cannot be seen

In the *right kidney* are found numerous tiny abscesses, which extend from the capsule in irregular lines down to the pyramids

The remaining organs are negative

The section of the femoral vein shows a thrombus adherent to the intima. There is no organization of the thrombus. The wall of the vessel is moderately edematous, and the fat and connective tissue about it also show edema, and are infiltrated chiefly with mononuclear cells.

The section from the muscle along the margin of the incision in the thigh shows great accumulations of polymorphonuclear leukocytes, in which are often large masses of cocci. The muscle-fibers adjacent to these infected foci are in places shrunken to mere threads, in other places they are swollen, hyaline and vacuolated, and the nuclei have disappeared.

The section of the heart shows the abscess in the fat extending down to the underlying muscle, and in the abscess are great masses of cocci. The myocardium adjacent to the abscess is beginning to degenerate.

Tricuspid valve. The section shows upon both surfaces of the valve close to the perforation an accumulation of fibrin and platelets in which are great masses of Gram-positive cocci. The valve beneath a portion of the exudate is entirely necrotic, and as one passes toward the free margin it is seen to be edematous and bacteria are found in the depth of the leaflet. Polymorphonuclear leukocytes are entangled in some parts of the exudate. Still closer to the free border of the valve there is only edema. The mass posterior to the leaflet is made up of platelets, fibrin, red blood-cells, and polymorphonuclears. Scattered throughout are great quantities of Gram-positive cocci.

In the sections of the lung there are found abscesses with great masses of cocci within them. Some of these abscesses appear to have had their origin in infected infarcts. In one of the large branches of the pulmonary artery is an infected thrombus, and the wall of the vessel beneath the thrombus is necrotic. In other sections of the lung there are characteristic infarcts in which are large masses of Gram-positive cocci.

The section of the spleen shows the typical picture of an acute splenic tumor.

In the kidney are found abscesses beginning in the pyramidal portion and extending up to the cortex. There has been considerable destruction of the tubules in the involved part, and large masses of cocci are found in the abscesses.

The remainder of the sections show nothing of especial note.

From the cultures of the abscesses in the lung hemolytic *Staphylococcus aureus* was obtained.

The anatomic diagnosis is Osteomyelitis of left femur, thrombophlebitis, left femoral vein, *Staphylococcus aureus* septicemia, with abscesses in the heart, kidney, and lungs, acute endocarditis—tricuspid valve (*Staphylococcus aureus*), with extension to and perforation of the septum membranaceum, acute splenic tumor, embolic infarcts of lungs, acute fibrino-purulent pleurisy.

CASE III

(L G History 13,648) A young, single woman, a dancer by occupation, entered the hospital September 11th, with the following history. Her right heel had been sore for twelve days, but she continued her dancing. A week later she had headache and was nauseated, and on the following day she collapsed while dancing. Went to bed two days before admission with a chill. Since that time she had had severe headache, vomiting, slight delirium, constipation, slight abdominal cramps, and a rash on her forearms.

Family History—Father, mother, and six brothers well. Two brothers died in childhood from rheumatic heart disease.

Past History.—Strong and healthy. Had rheumatic fever ten years previously without known heart involvement. Tonsillitis six months ago. Menses normal. Last period four weeks ago. No leukorrhea.

Physical Examination—Temperature, 105.6° F, pulse, 120, respirations, 28. Blood-pressure 108/65. Well-nourished and developed young woman, seriously ill and prostrated. Restless and irritable, any movement causing pain. No jaundice, dyspnea, or cyanosis. Scalp clean and dry. Pupils regular, equal, and react normally. No palsies. Ears showed no discharge and the drums were normal. Teeth in good repair.

Tongue coated and dry Lips cracked Fauces, pharynx, and tonsils reddened On the inner surface of the left cheek there was a small hemorrhagic blotch Neck was stiff, but not retracted The thyroid was not enlarged No lymphatic glands palpable The lungs showed only a few fine râles in right axilla and at both bases

Space

Heart, 2- 6 cm

At right, 3- 9 "

Sternal, 4-11 "

Margin, 5-12 "

Action regular There was visible pulsation in second left space No thrills Sounds were rather loud There was a soft systolic murmur at the apex, and at the base there was a second systolic murmur, loudest in the second left space, not transmitted upward

Abdomen was symmetric There was resistance to palpation, but no rigidity or tenderness Liver, spleen, and kidneys not felt

The knee-jerks were present, but sluggish No Kernig, Babinski, or clonus Musculature of legs very well developed and firm

The skin about the toes and heels was thickened and caloused and in places reddened The right heel was moderately tender, but there was no swelling and no general redness, although there were some small red spots, 1 to 2 mm in diameter, which were partly erythematous and partly hemorrhagic

On the lower part of the forearms and over the dorsum of the hands were several erythematous patches, 3 to 4 mm in diameter, which did not fade out entirely on pressure

Vaginal examination showed nothing abnormal except a slight, yellowish-green discharge Rectal examination negative

Blood count W B C 11,800, polys 76 per cent No malaria organisms

The diagnosis made on admission was "Septic endocarditis"

Course—September 12th There is slight ulceration of the gums Right ear shows a little redness of upper wall of the canal and the upper margin of the drum

Lumbar puncture Clear fluid showing 43 cells, polys 31 per cent, lymphos 50 per cent, endothelial 19 per cent Culture shows *Staphylococcus aureus*

September 13th Last night had spasmodic contractions of right arm which seemed to be confined chiefly to the muscles about the shoulder

This morning she is semicomatose Temperature, 104.2° F, pulse, 136 Neck rigid Tache cérébrale The red spots on hands and forearms are deeper red and hemorrhagic Abdomen is distended, but not rigid There is a suggestive Kernig No ankle-clonus or Babinski

W B C 16,600, polys 81 per cent. Blood-cultures taken on admission and on the 12th show *Staphylococcus aureus* There are several petechiæ on the neck She has developed a slight purulent conjunctivitis Ears are normal On questioning mother it was found that the sore on her heel had been pricked, rubbed, and covered with colored stockings, and at times had contained pus Right arm flaccid

September 14th Comatose Temperature, 106° F, pulse, 150, respirations, 38 Over neck, chest, upper abdomen, arms, and on conjunctivæ are many fresh petechial spots Right arm is still flaccid and she does not move her right leg Kernig more marked Neck stiff Lungs show râles throughout both lower lobes The systolic murmur at the base of the heart is louder Spleen not felt

Lumbar puncture done yesterday showed turbid fluid, 120 cells with 83 per cent polys, and 17 per cent lymphos, and, by culture, a *Staphylococcus aureus*

Blood and spinal fluid Wassermann negative Two further blood-cultures showed *Staphylococcus aureus*

The urine showed a trace of albumin and sugar and many granular casts

Autopsy 8387 The findings in this case are best summarized by giving the anatomic diagnosis Persistent thymus gland, small abscess of right great toe, *Staphylococcus aureus* bacteremia with metastases, *Staphylococcus aureus* vegetative endocarditis (mitral and aortic), bacterial emboli of heart muscle, spleen,

liver, pancreas, kidney, and adrenals, abscesses in heart muscle, pancreas, kidney, and mesentery, infarcts of spleen, kidneys, and mesentery, hemorrhages into skin, pleura, pericardium, heart muscle, esophagus, stomach, pelvis of kidneys, and ureters, bronchopneumonia, acute and chronic pleurisy, hydrothorax and ascites, acute bronchial lymphadenitis, acute splenic tumor, acute embolic nephritis. Brain not examined.

The organ of special interest in this case is the heart. It weighs 280 grams. There are numerous petechial hemorrhages beneath the pericardium. The foramen ovale is patent. The right auricle and ventricle are negative except for a few subepicardial petechiæ. The pulmonic and tricuspid valves are negative. The mitral valve is not thickened, but there are upon it soft, friable vegetations which extend back from the free margin to the line of closure. The chordæ tendinæ are not involved. These vegetations are light yellow, they are rather flat and condylomatous-like. The largest of the vegetative masses is on the anterior leaflet. There are vegetations similar to these on the aortic valve. Neither of these valves show ulceration. In the myocardium are small hemorrhages and abscesses.

The microscopic examination revealed numerous bacterial emboli and abscesses in the myocardium. Many of the arteries are completely plugged by masses of bacteria. The section of the mitral valve shows that there has been considerable destruction, that there is an acute fibrinopurulent exudate upon the surface, and in the exudate are great masses of cocci. An artery near the base of the valve is plugged with a bacterial mass.

It is of interest that this case showed an abnormally large thymus, and the individual had the hair distribution of the opposite sex.

CLINICAL DISCUSSION

The outstanding fact about these 3 cases is that all suffered from a general septicemia or bacteremia, and that the endocarditis was but an incident, though an important one, in the general picture. Now it has been recognized for at least thirty

years that the bacterial endocarditides could be divided into two main groups

The first group has been called primary or cryptogenetic, the essential point being the fact that the only important lesion is in the endocardium. This central lesion acts as a distributing focus, keeps up the bacteremia permanently or transiently, and is the source of emboli. In this group there are the acute cases, lasting, at most, only a few weeks, and the chronic cases, whose duration is measured in months. Practically all of the chronic cases are caused by the non-hemolytic streptococcus, a very few by the influenza bacillus. Other bacteria, as causative agents, are so rare as to be practically negligible.

The important organisms in the acute cases are the hemolytic streptococcus, pneumococcus, Staphylococcus aureus, and gonococcus.

The other main group has been called secondary. These cases are characterized by the fact that the endocarditis is only a part of the general septicemia and that there are one or more foci in addition to the one in the endocardium, feeding bacteria and emboli into the blood-stream.

Having thus oriented ourselves, we see that the first 2 cases today belong to this second group, while the third case is primarily an acute form of the first group. It rapidly becomes a member of the second group, however, as do all of the Staphylococcus aureus cases. For even if we conceive of a primary localization upon the heart valve from some unknown original focus, the resulting bacteremia and emboli rapidly light up purulent foci in other parts of the body, and we then have multiple foci furnishing bacteria and emboli to the circulation.

You may well ask why we should trouble ourselves about this type of endocarditis if it is only an incident in a general Staphylococcus aureus septicemia. There are several answers. In the first place, we are all anxious to make exact diagnoses. In the second place, there are some cases, such as the last one today, where it was possible to make a diagnosis of "septic endocarditis" as the main condition. More intensive study of this group will allow us, I am sure, to make the diagnosis

of the causative organism In the third place, such study will aid in a better understanding of endocarditis, its mode of origin, and the body's defensive mechanism The latter is especially important, for it is a well-known fact that only a small proportion of the cases of *Staphylococcus aureus* bacteremia develop endocarditis, 20 per cent in this hospital Why, in the presence of such a virulent septicemia, do the great majority of heart valves escape? And finally, the ability to determine the presence or absence of such an endocarditis has a very definite bearing upon the prognosis Thus we know that approximately 75 per cent of cases showing *Staphylococcus aureus* bacteremia die (Libman, Soper) Knowing this, we can immediately tell the patient's friends that he has in general a 25 per cent chance of recovery But the presence of an endocarditis reduces his chance to zero And I believe that further study will enable us to pick out the cases of endocarditis among the *Staphylococcus aureus* bacteremias, although we certainly cannot do it with any degree of confidence today

If we consider these cases from the standpoint of the septicemia, the embolic phenomena, and the cardiac signs, certain points will be brought out which we can verify or disprove in future cases

Septicemia—We cannot diagnose *Staphylococcus aureus* endocarditis without the knowledge that there is a *Staphylococcus aureus* bacteremia Naturally we depend upon blood-cultures to settle this point, but this involves a delay of from twenty-four to thirty-six hours, and it dulls our diagnostic wits and our powers of observation to depend entirely upon the laboratory We should form our surmises, based upon facts, and allow the laboratory to verify or refute them We need not go into the picture of septicemia Our cases today have furnished you with it in all its virulence The point which concerns us is whether there are any means at our disposal, apart from blood-cultures, of determining the etiologic agent The occurrence of past or present *Staphylococcus aureus* infections is of the utmost importance Our experience has led us to feel that the history of boils in any case presenting the picture

of septicemia cannot be disregarded. In the first 2 of our cases such a history was *obtained*, but was not *volunteered*. Another lesion of great value is osteomyelitis. Knowing as we do that such an infection of the bone is almost always due to the *Staphylococcus aureus*, we are almost certain that an accompanying septicemia is caused by the same organism. Such proved to be the case with 2 of our patients. These are the only two types of infection which we can definitely connect with the *Staphylococcus aureus*.

There is another sign of great importance in determining the type of bacteremia, and that is the skin lesion, which will be dealt with under the embolic phenomena.

Having determined by these means or by blood-cultures that there is a *Staphylococcus aureus* septicemia, we have established the possibility of an endocarditis due to this organism. We know that such an endocarditis will occur in one-fifth of the cases, but as yet we do not know of any special features of the septicemia which indicate an endocarditis with the exception that such a septicemia without a known local lesion or with symptoms out of all proportion to the local lesion is highly suggestive of endocarditis. Thus in our last case the trivial foot lesion is insufficient to account for the gravity of the symptoms, and without other recognizable foci our attention is directed to the heart.

The course is rapid in the fatal cases, generally only a few days, with an outside limit of five weeks.

Embolic Phenomena—*Staphylococcus aureus* septicemia is an embolic disease par excellence. The emboli are purulent and spare no part of the body. Those to the skin are quite characteristic. While not described as present in 2 of our cases, they were present in the third. The typical lesion is usually described as a petechia with a tiny yellowish-white center. As a matter of fact, they are minute yellowish abscesses surrounded by a small red halo which does not entirely fade out on pressure. Once seen, they can scarcely be mistaken for any other lesion. They are practically diagnostic of this type of septicemia, but do not necessarily indicate an endocarditis.

Another type of skin lesion is the irregular ecchymosis. These lesions were quite definite in a case seen here some time ago. One of the lesions was excised and presented the following microscopic picture. "Section shows a small area with a necrotic center surrounded by an area of marked infiltration with polymorphonuclears. The connective-tissue cells show a marked hyaline degeneration and there is considerable edema. The blood-vessels are filled with red cells, fibrin, and numerous white cells. The skin appears normal. Gram stain shows numerous staphylococci in the necrotic area. They are especially numerous about the blood-vessels, which appear to be plugged by a solid mass of them."

In addition to these lesions, Libman has reported numerous milary abscesses in the hairy scalp.

There may be emboli to almost any part of the body, giving the characteristic signs and resulting in a purulent focus. At least one embolic aneurysm has been reported (Libman). Urine cultures frequently show the *Staphylococcus aureus*.

Abscesses in or beneath the muscles are highly suggestive of this organism.

Cardiac Signs—We have learned previously that non-hemolytic streptococcus endocarditis is almost always engrafted upon a previously damaged heart valve. With the *Staphylococcus aureus* this is not true. None of today's cases showed evidence of an old endocarditis, and this holds true for most of the cases.

Perhaps the most important aid in diagnosis of an endocarditis, once a *Staphylococcus aureus* bacteremia is established, is the development of a new cardiac murmur or an alteration in the quality of an existing murmur. This is especially true for diastolic or presystolic murmurs. It is scarcely necessary to point out the difficulty of differentiating a functional from an organic systolic murmur. It is, therefore, most essential for us to make very careful and repeated examinations of the heart in these cases, noting our findings accurately, for it is *change in the signs* which is generally of greater significance than the *signs themselves*.

The development of a pericardial friction-rub is naturally evidence of cardiac involvement. It is due to a myocardial abscess reaching the pericardial covering, and while such abscesses may occur without endocardial involvement, their presence lends weight to the possibility of endocarditis.

We have pointed out some of the known facts in order to stimulate your interest in these cases and to encourage you to help in the future to round out the picture. I would especially ask you to consider the pathology carefully, as that is the foundation upon which you must build your knowledge, and these cases show the characteristic lesions.

You will find the best recent review of the whole general question of bacterial endocarditis by Simons in *The Quarterly Journal of Medicine*, 1913-14, 7, 291. This article contains a survey of the literature.

DISCUSSION OF PATHOLOGY

In reviewing our autopsy records of *Staphylococcus aureus* septicemia, of which there have been 25, I have found 2 other cases with involvement of the valves of the heart besides the 3 reported here.

One of these cases was a boy, aged twelve (Autopsy 8890), who was admitted to the hospital complaining of pain in left arm and shoulder, of five days' duration. Physical examination revealed an abscess of the left scapular region, which was incised and pus was found extending down between the deltoid and trapezius muscles. Culture of this pus showed hemolytic *Staphylococcus aureus*. The blood-culture was positive for the same organism. The heart was very rapid, with a roughened first sound over the sternum opposite the third costal cartilage. There developed gangrene of the left great toe, and numerous petechiæ appeared in the skin. One of these petechiæ was excised, the histologic examination of this piece of tissue has already been given to you by Dr. Lamb. The temperature gradually rose, and he died on the fourth day after admission to the hospital, which was nine days after the onset of the disease.

The autopsy findings were Abscess of left scapular region, osteomyelitis of left achromium process, Staphylococcus aureus septicemia, acute endocarditis (Staphylococcus aureus), abscesses in heart, lungs, liver, and kidneys, septic spleen, gangrene of left great toe, multiple milary cutaneous abscesses

The heart in this case showed many small abscesses in the myocardium, especially of the left ventricle and the papillary muscles. On the left cusp of the mitral valve was a small, friable vegetation along the line of closure and extending down on the chordæ tendineæ. In the tricuspid valve were small petechiæ in all the leaflets.

A section of the mitral valve showed an exudate upon the surface in which were numerous Gram-positive cocci. Upon the surface of the tricuspid valve were masses of similar cocci, none, however, were seen in the depths of the valve. The myocardium was extensively involved by abscesses.

The other case in this group was a man, age sixty-five (Autopsy 8357), who was admitted to the hospital on two occasions with a history of nephritis and cardiac decompensation. At the time of his last admission there was an abscess of the left buttock which finally healed completely. Some time later the edema of the extremities and scrotum became very marked, and on two occasions the scrotum was incised, with considerable relief from the edema. A week before his death the whole lower portion of the scrotum became gangrenous. His temperature, which previously had varied between normal and 100° F, gradually rose to 103.5° F.

The findings of interest to us in the autopsy are centered chiefly in the heart, which weighed 770 grams. The right auricle and ventricle and the tricuspid and pulmonic valves were essentially normal. The endocardium of the left auricle was scarred in places. The mitral valve was thickened, and in both leaflets there were hemorrhagic areas, and the surface over these appeared to be somewhat ulcerated. The wall of the left ventricle was increased in thickness. The aortic cusps were moderately sclerotic and stiffened, and the endocardium

beneath them was reduplicated, forming small pockets. The myocardium was brownish-red in color.

The section of the heart muscle showed a small abscess, the center of which was formed by a vessel filled with cocci. There were other smaller similar areas scattered throughout the myocardium. In the mitral valve there were large areas of hemorrhage, which in places reached to the endocardium covering the valve. A little distance from the hemorrhages the surface of the valve was ulcerated and irregularly covered with fibrin and masses of cocci.

Unfortunately a blood-culture was neither done during life nor at the autopsy, but the presence of Gram-positive cocci in numerous abscesses in practically every organ of the body stamps this as an undoubted case of *Staphylococcus aureus* sepsis.

There are many points of interest in this group of cases. You will note that 2 of these occurred in individuals of the so-called status thymicolymphaticus type, 2 were secondary to acute osteomyelitis, and 2 followed either infections of the skin or the soft parts. In 1 case the portal of entry was not evident. In all of these cases there were typical embolic lesions—multiple abscesses—in various organs. The blood-stream is most probably contaminated by infected thrombi in veins either at or near the site of the primary focus. This was clearly demonstrated in the second case reported here.

In this small series the various valves of the heart were involved, with the exception of the pulmonic. The mitral and tricuspid valves were affected three times, the aortic twice, and in 2 of the cases the valvular involvement was multiple. The earliest change in the valve from a study of these cases appears to be hemorrhage into the substance of the valve, with a small accumulation of exudate upon the surface of the leaflet. Even in the early stages there is actual necrosis of the valve, and bacteria are found in the substance of the valve as well as in the exudate upon its surface. Apparently there form very quickly over the infected portion of the leaflet large, bulky, soft or crumbly, thrombotic masses varying considerably in color.

Some of these have been described as being reddish gray, others pinkish, and some yellowish white

The necrosis of the valve, it would seem, advanced with actual liquefaction, and may be so extensive that perforation of the leaflet occurs, and the opening in the leaflet may be plugged by the thrombotic mass

Another feature is the tendency for the process to extend to the adjacent myocardium, and abscess formation with discharge of the abscess content into the blood-stream may result either in the formation of a small cavity in the heart wall or, as in one of these cases reported here, in perforation of the septum. These thrombotic masses upon the valves are heavily infected and are another fertile source for infected emboli. The lesions in the myocardium are chiefly abscesses such as are found in other organs

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CLINIC OF DR HARLOW BROOKS

UNIVERSITY AND BELLEVUE HOSPITAL MEDICAL COLLEGE

THE TREATMENT OF PNEUMONIA

Based on a Broad Clinical Experience and a Description of Measures which One Will Be Called Upon Most Frequently to Use, Knowledge Not Derived from the Laboratory Nor from the Dead-house, but from a Study of the Disease as it is Seen Clinically in the Ward and By the Bedside of the Private Patient

GENTLEMEN At this period of the year the treatment of pneumonia is a very timely and important question There is no standard, routine, or "ward" treatment for pneumonia There is probably no other medical condition in which treatment must be more determined by the individual patient and case than is true of pneumonia The more individualistic the treatment, the more successful its results

It has been stated that the successful treatment of pneumonia is more dependant upon nursing than upon medical skill This is about one-third or, perhaps, one-half the truth As a matter of real fact, successful treatment depends chiefly on the prompt and individualistic application of many well-established medical procedures applied at the correct time, not too soon, not too late, and the more definitely these measures are adapted to the definite case under study, the more successful the result Great versatility, a broad grasp of the whole armamentarium of the well-equipped physician is demanded, and promptness of action, decisive procedures are often required On the other hand, a lack of meddling therapeutics, a letting of the patient be, is perhaps even more needed at times

We shall have very little to say of the specific treatment of pneumonia today As yet this is a very definitely limited

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and circumscribed field, but I believe that your generation, certainly that which is to follow you, will have put in its hands a weapon perhaps as effective in pneumonia as antitoxin is in diphtheria or mercury in syphilis. That time has not yet arrived, and in our talk today I shall merely attempt to give you, as it were, the general consensus of therapeutic opinion of the present-day generation of practitioners. I shall have little to say of theories, of hopes for the future. I shall try to point out to you, in so far as a broad clinical experience with this terrible disease has schooled me, those measures which you will be most frequently called upon to use. This knowledge has been mostly derived not from the laboratory, nor even from the dead-house, but from a study of the disease as we see it clinically in the camp, field hospital, in the ward, and by the bedside of the private patient. Perhaps it is meet for me to at first confess that this experience has taught me more humility than pride, and more caution and respect than positive opinion and definite conclusion. Nonetheless I feel quite confident that the victories of the physician are never more certainly won elsewhere in the practice of medicine than is often the case with pneumonia.

As you know from the teachings of your pathologist and of your bacteriologist, there are several, even many kinds of acute pneumonia, but in so far as the therapist is concerned much of this detailed knowledge is unnecessary, even inadvisable, if it be secured at the sacrifice of the patient's rest, through a delay in treatment, or if your basis of treatment be determined by theoretic conjectures and busy-body and exhausting physical examination.

Remember at all times that the chief point in the management of acute pneumonia is that you are treating a patient with an inflammatory condition of his lungs rather than some specific, definite, and unmixed infectious process. Please do not misunderstand me to suggest that you neglect proper physical examination, the use of the fluoroscope and x-ray, the thorough study of the sputum, the blood chemistry at times, the study of the expired air and of all phases of disturbed lung

prefer. Never forget to seriously consider the comfort of the patient in the treatment of this disease

As to the outdoor treatment of pneumonia, I am personally very partial to it, but it depends much on weather conditions, customs of the patient, and somewhat on the extent and type of the infection. That preferable, however, is usually a matter easily determined. Move the patient's bed out on the veranda, or open all the windows, and if his cyanosis or dyspnea are relieved, this is the right thing, he will probably rest better, eat better, excrete better, and get well faster and in more comfort. If, on the other hand, he becomes more dyspneic, if his hands and feet and the tip of his nose become cold, if he becomes more restless or delirious, move him back into his room, see that abundant air is present, but have the room well warmed. Be very cautious how you expose the outdoor patient in examinations, in the use of the bath, the urinal, and bed-pan. Chilling of the skin surfaces is quite as capable of doing harm as good. Very few of us are alarmed now by the high temperatures of pneumonia, and very few of us use other agencies for the reduction of temperature than sufficient ventilation. My personal results in the use of hydrotherapeutic measures other than cleansing the body by gentle and not too tiring sponge-baths, tepid rather than cold, has not been satisfactory, and I have studied under and observed closely the methods of Dr. Baruch, who we all admire and reverence because of his intimate and skilful adaptation of hydrotherapy. I had the benefit of his assistance, instruction, and cooperation in my pneumonia wards at Camp Upton in 1917, but it has but crystallized my former ideas on this subject.

May I digress right here and say that I believe that the sputum should be secured and typed just as early as it can be obtained, even before the diagnosis is absolute, for I know that while the use of Type 1 serum in Type 1 pneumococcus infections is a splendid thing, it is not 100 per cent perfect any more than any other therapeutic measure. I speak of this here for the reason that I must insist that if you contemplate the use of serum, you must first type the sputum, for I am

pressure is usually high, though it may fall at any time with a failing heart muscle. These patients are usually full-blooded adults, the overly plethoric and overly vigorous, though sometimes the measure seems also indicated where the lung involvement is very great. I rather suspect that in all such cases there is an overburdening of the right side circulation. Most of such instances are much improved at least symptomatically by a timely venesection. May we thus abort or terminate an attack of pneumonia? I cannot answer this question either for or against. I have seen some instances in which this seemed to be the case, but so also have I rarely seen cases of apparently advanced involvement suddenly terminate and deservescence without anything being done.

Just a few more words as to the specific treatment of pneumonia. I have already said what I wish to say in regard to the use of Type 1 serum in Type 1 cases. May I be permitted to say that I hope that eventually a serum or a vaccine may be discovered which will be equally as beneficial in other pneumococcus types, in the streptococcus cases, and so on. As many of you know very extensive clinical experiments along this line are now being conducted in Bellevue Hospital. I have great confidence in Russell Cecil, who is mostly responsible for this work, and I am correspondingly hopeful, but it has thus far not passed beyond experiment, and the mortality rate in pneumonia is such a variable thing under different environment and in different epidemics that we must be very cautious in our conclusions.

Foreign sera are being used. Joseph Miller and Joseph Capps, of Chicago, have something to say in favor of these experiments, and their opinions carry as they must considerable weight, but, naturally, such men are very cautious as yet in their claims. Vaccines are being used particularly in streptococcus and in influenzal cases. As these experiments are being conducted they are certainly doing no harm in the hands of the careful men who are mostly making these studies, but beware as yet of commercialized specific products.

Dr Solis Cohen, of Philadelphia, a most experienced and

digitalis or of some member of this group in the pneumonias, at least in those cases which show circulatory embarrassment. A considerable group of us, and I number myself as of this party, feel that cardiac failure is of so frequent occurrence in this disease that a digitalization prior to the appearance of symptoms demanding its exhibition is an advisable practice. Of this group there are those who believe in digitalization by the rapid method, that is, by the administration of maximum doses very early in the disease, arguing that thereby they lessen their mortality rates by preparation of the heart for its inevitable stress. Others of us use it in most cases. I myself use it practically universally, except in children, or where the tissue involvement is slight, but I introduce the treatment by medium-sized doses gradually increased or prolonged until evident signs of digitalis effect are reached, cutting it down or out then except where circulatory strain is evident, on which occasion it is continued or even increased. In cases which from the outset show signs of circulatory distress, or in which a defective heart is known to exist, I digitalize by the rapid method.

I am strong in my belief that we are thus able to materially reduce our mortality lists in pneumonia. In a review which I made of over 5000 protocols of cases dying in the American Expeditionary Forces from pneumonia I believe that I found abundant evidence justifying this use of digitalis in pneumonia and bearing us out in the assumption that harm is rarely or never caused as a result of the method. Perhaps I am too strong a partisan of this method to give you a fair idea of it, but the very close touch which I was able to bear to literally thousands of cases of pneumonia in the army during 1917-18-19 causes me to feel that I am doing you and many of your clients a real service in most heartily endorsing this step in the management of your pneumonia cases.

Just a very few words as to the forms of digitalis which I have best used. The tincture, a physiologically tested and well standardized product, is my favorite, but I have used pulverized leaves, the infusion, digitol, digifoline, digalene, and other intravenous and hypodermic forms also successfully. You

of this problem, but he cannot know too much of them if he will treat pneumonia well. Again, however, I wish to point out to you the even greater danger of overtreating your cases. My own repertoire of drugs which I employ in most cases is extremely small. Digitalis is used in the average case however.

We older men all remember when the sovereign remedy in pneumonia, as in other conditions, at the time was oxygen. Then the method died a natural and little lamented death. The manufacturers, in their attempts to reestablish its popularity, ceased to paint the cans blue, so associated had fatalities and the "blue can" become in the minds of both patient and physician. Well, the oxygen treatment has been born again. It is urged once more, now on a chemical basis, because of a very narrow and ill-defined theory of the respiratory chemistry in pneumonia. It will take more than theory to reestablish it again in the minds of the experienced physician who during his intern days saw its failures and its very rarely beneficial results. It is of benefit in my opinion in certain cases of severe cyanosis due for the greater part to very extensive lung involvement, though it is by no means generally acknowledged as of value even here. It is entirely without effect in cardiac failure in pneumonia, no matter how efficiently it may be administered. It causes marked desiccation of the mucous membranes of the upper respiratory tract, and in my opinion is of far less value than the open window and a fan in the hand of a persistent nurse.

Of course it has been found that acidosis plays an important part in the death-rate from pneumonia. Again a contribution from the chemical laboratory. There is little doubt that the alkalis, particularly sodium bicarbonate, are useful when defective renal excretion becomes apparent from any cause. There appears little clinical utility for the method, however, except in such instances. If administered in a laxative form, as, for example, the oxid of magnesium, the laxative effect is doubtless useful, there are, as a matter of fact, few disease conditions which are not benefited by clearing of the bowel, and where the method does not cause too much annoyance and dis-

propaganda of zealots or theologians I have no opinion to express on the use of alcohol as a beverage, my "clinical experience" in this line is very limited, but on the utility of it as an agency for the treatment of the sick, you and I are morally responsible if we permit the myopic zealot to wrest from our hands any agency or weapon which is of so real benefit in many disease conditions

I am entirely out of patience with the tendency shown in some schools to teach students that the treatment and relief of mere symptoms in the course of any disease is foolish, unscientific, and beneath the dignity of the physician This is a particularly fallacious doctrine as regards pneumonia As a matter of fact, the greater part of our active treatment in pneumonia except by the use of the sera and vaccines is symptomatic and nothing more The relief of the symptoms is often the deciding point between the life or the death of the patient Of course you must not strive to relieve symptoms to the point of doing the patient harm, of lessening his resistance against the infection, or of favoring the progress of the disease process The physician who gives overdoses of morphin or codein in pneumonia merely to give comfort is quite as unartful, inconsistent, and unscientific as he who entirely refuses these most useful drugs when their adequate exhibition will quiet an exhausting cough, a distressing and agonizing pleurisy pain, or bring sleep to a tired and perturbed brain Of course you will not use the morphin to the point of depressing the respiratory center, increasing the cyanosis and real dyspnea, but if you do not use it for its therapeutic effect in very many of your cases of pneumonia you will permit much unnecessary suffering, and will favor the progress of the disease and the loss of your patient's life because of the exhaustion which pain, lack of sleep, or irritating cough bring so frequently to the pneumonic

Tympanites is a most serious symptomatic manifestation in many cases of pneumonia It seems particularly frequent, distressing, and dangerous in cases complicated by a diaphragmatic pleurisy, in many severely toxic cases, where the meninges are involved and doubtless in many other instances and condi-

peusis which the good physician must explore in his attempt to give the patient relief.

I have but begun to indicate to you the symptomatic conditions which arise in pneumonia and which demand the best that is in you in the way of therapeutic skill, and my hour is nearly done. May I close this talk by reiterating the importance of the study and management of symptoms and of the individual in this disease?

Do not overtreat your patient. Use just as few drugs and just as many other physical measures as are demanded only. Disturb your patient just as little as possible. Do not examine him too frequently or too thoroughly just to satisfy your own curiosity. Try to bend every bit of knowledge which you possess to the relief of symptoms, to the support of the circulation, the promotion of excretion, and of rest in your case. It is very true that as yet we have very little to offer in the way of real treatment of pneumonia as a specific disease, but we have a tremendous field of effort which we may cultivate for the patient's relief. Stay with your patient as much as possible. Shape every sign and symptom to his benefit—that is the sort of "nursing" that cures pneumonia. Your close study and the application of your general knowledge of disease and therapeutics applied to the crisis as it develops may win the fight. You will, I doubt not, save many cases which would have otherwise died by just this individual study which I have suggested to you. You may not "cure pneumonia," but you can many times give life where but for you and your knowledge and effort death would have taken place.

Physiologists have taught us that the circulation depends upon the proper action and coordination of the heart and arteries and veins, the most important of these factors being the intermittent pumping action of the heart, and the elasticity of the arteries, which converts the intermittent systolic output of the heart into a continuous stream. Important, too, is the peripheral resistance, which maintains a more or less constant head of pressure, and which has been thought of as dependent largely upon the degree of contraction of the smaller arterioles. In more recent years two other factors of importance have been emphasized, one, and the least well understood, is the elasticity of the tissues, the other, and it is the factor to which I wish to pay particular attention in this clinic, is the capillaries themselves. If it were true, as we used to think, that the capillaries are merely passive agents, and that the blood flow within them is determined by the state of the arterioles that supply them and the venules that drain them, a further discussion would be unnecessary. We have learned, however, that the capillaries take an active part in the distribution of the blood to the tissues by means of their inherent power of contractility and dilatability.

A very striking example of the importance of this action of the capillaries is their behavior in the condition known as "shock." For an understanding of this mechanism we are indebted to Dale and his co-workers and to Cannon. In brief, they have demonstrated that in "shock" there is a paralysis of the capillaries, as a result of which they become dilated and the blood becomes stagnant within them. When very many of the capillaries are thus affected they form a great reservoir of stagnant blood that is withdrawn from the circulation, so that there is insufficient blood in the heart and arteries to properly maintain the circulation. The injection of histamin into the body produces similar results and by means of it the mechanism of the reaction may be more carefully studied. Small doses of histamin, when injected, produce a rise in blood-pressure due to a contraction of the smaller arterioles. When larger doses are given there is still a primary rise in blood-pressure, which is soon exhausted, however, by a tremendous

THE MORPHOLOGY OF THE CAPILLARIES

It is difficult to define the normal appearance of the capillaries at the base of the finger-nail. Figure 191 represents, perhaps, the usual picture in healthy individuals. Here are seen one or two rows of simple loops just proximal to the cuticle, and below them many rows of shorter, more comma-shaped vessels. The difference in the appearance of these capillaries is due to the fact that in the first row the papillæ of the skin are flattened out so that the vessels are viewed running horizontally, while in the lower layers, where the papillæ are present, one sees only the top of the vertical capillary tuft. It is this arrangement of the papillæ that makes the finger the ideal site for the study of the capillaries, for it is only in the long loops that the blood flow and the blood-pressure can be properly studied. Over the rest of the body the capillaries present the appearance observed in the lower layers of the finger. Some German observers, particularly Weiss, have given elaborate descriptions of the capillaries in disease, and have drawn rather far-reaching conclusions from their studies. I shall try to show that in the present state of our knowledge most of these deductions are unjustified.

Weiss and some of his co-workers have described the following capillary pictures in disease. In arteriosclerosis the capillaries are present in normal numbers, but they are longer and more tortuous than in healthy individuals. In nephritis, both acute and chronic, the number of capillary loops is increased, and the individual vessels are longer and wider than usual and are greatly looped. In diabetes there is a point of dilatation at the junction of the arterial and venous loops of the capillary. With venous stasis the venous end of the capillary is greatly dilated. In both adults and children with vasomotor instability the capillaries are long and tortuous. This obtains particularly in patients with acrocyanosis.

These observations would be of real value to the clinician if he could be assured that the morphologic variations of the capillaries were of constant significance. Personal studies have convinced me that such generalizations can be made only with

of our knowledge we cannot generalize and say that a certain capillary picture is pathognomonic of a certain disease. The most that we can say is that in diseases in which the vascular system is affected the capillaries tend to change in appearance, and that this change manifests itself chiefly in an increase in length and tortuosity of the vessels.

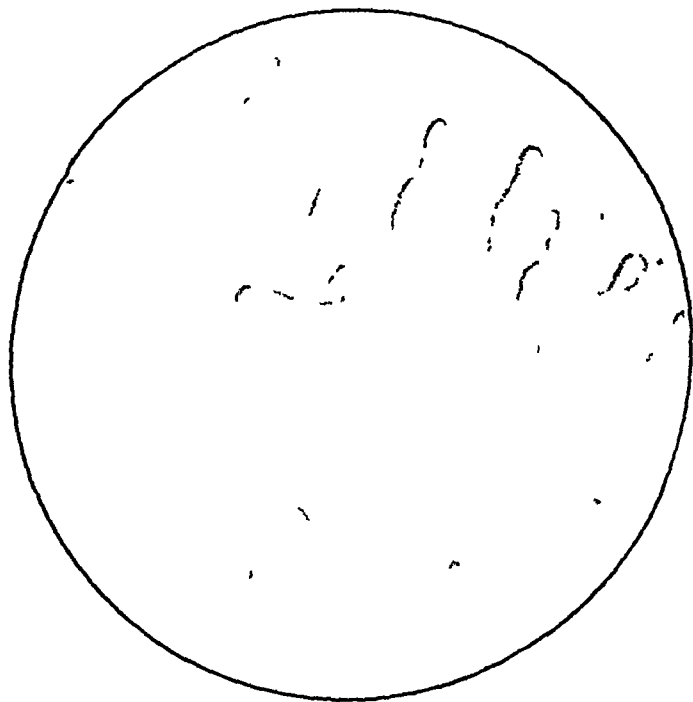


Fig. 192 —Normal individual. Long numerous irregular capillaries showing the venous loop in some entering the subcapillary venous plexus.

It will be of interest to recall at this point the similar change that the arteries undergo in disease. Disease of the arteries exhibits itself to the clinician either as a thickening of the vessel wall or as an increase in length and increase in tortuosity of the artery. The tortuosity is consequent on the lengthening of the vessel, for since the distance between the origin and termination of the artery remains the same, an increase in length

laries can be observed I have discussed this point elsewhere and wish to emphasize here only that the term "capillary pulse" is a misnomer. The phenomenon is probably due to an increased pulsation of the small arterioles, and possibly of the venules.

The blood flow in the capillaries of the normal individual may be modified by various extraneous factors. Thus cold will retard the flow, while heat will accelerate it. This can readily be observed after cooling and warming the hand. When the capillary flow becomes slow the column of blood no longer has the normal continuous and uniform appearance, but is broken into segments separated by colorless areas. This may be called a "granular streaming." It is rarely observed in the normal circulation, and when present in many capillaries indicates some disorder of the capillary circulation. The flow of the blood in the capillaries may be artificially modified either by inflating a blood-pressure cuff that has been applied to the arm, or else by inflating the capsule of Danzer and Hooker's microcapillary tonometer. Under such conditions the capillary circulation may be altered at will, and the variations in the flow may be studied at leisure.

In certain disorders of the circulation a modification of the capillary flow may be observed. Probably one of the most frequent abnormalities observed is "granular streaming." This is seen not only when the flow in the capillaries is slowed but also when they have undergone a morphologic change. Thus it will be noted in patients with venous stasis due to myocardial insufficiency, as well as in those who exhibit the abnormal capillaries seen at times in arteriosclerosis and nephritis. Not infrequently complete stasis may be observed in several capillaries. The blood accumulates in the venous portion of the capillary, which becomes swollen, while the afferent arterial loop may empty itself almost completely. Then suddenly the venous loop empties itself and the blood flows again through the whole capillary with an increased velocity. These studies show us how abnormal the capillary flow may be in various circulatory disorders, but a further elucidation of the

and of the parts unseen we can judge only by analogy. Moreover, the interplay of the many factors that sustain the circulation is so complex that the greatest circumspection must be observed in drawing generalizations.

THE CAPILLARY BLOOD-PRESSURE

The capillary blood-pressure can be readily measured with Danzer and Hooker's microcapillary tonometer. It is important

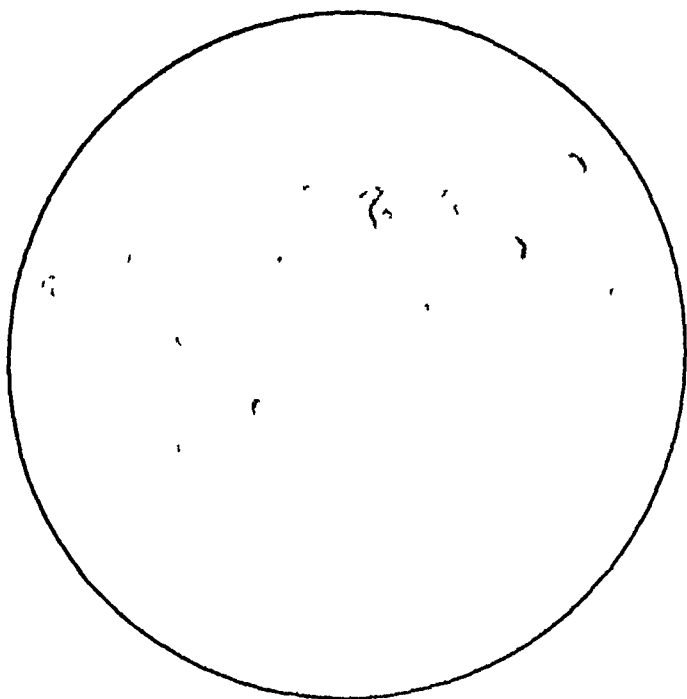


Fig. 193—Rheumatic mitral stenosis B P 184/100 Slight clubbing of fingers Capillaries numerous and rather tortuous Capillary pressure 4 to 10 mm Hg

to keep the hand at heart level during the estimation in order to avoid the hydrostatic effect of the column of blood. The figures for normal individuals lie between 15 and 30 mm. of mercury. Not all of the capillaries of one finger or of different

are above 30 mm Hg, one may be sure that the capillary pressure is high, when they are below 15 mm Hg, the pressure is low

I have had the opportunity of studying the capillary pressure in a series of patients with hypertension. The results are reported in detail elsewhere. We find that the cases fall in two

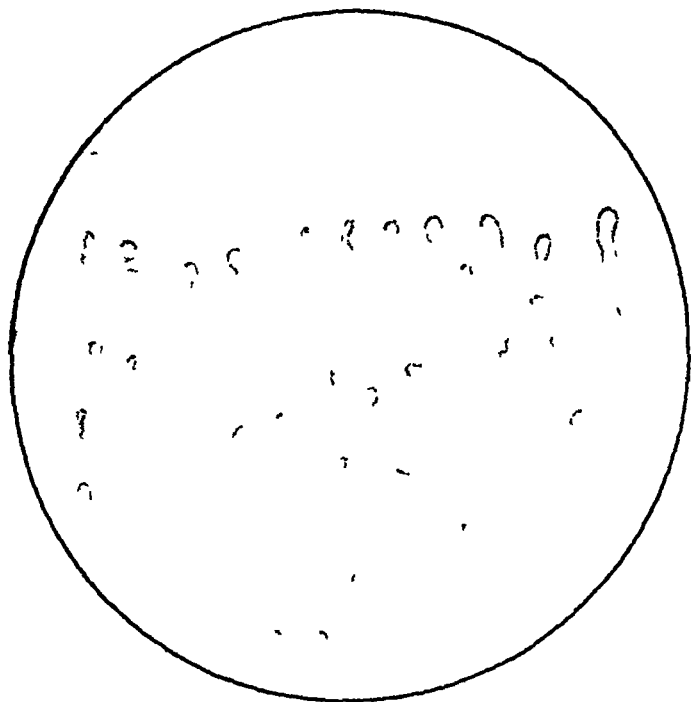


Fig 195—Mitral stenosis, auricular fibrillation, compensated B P 105 systolic. Capillaries numerous, rather thick. Many layers of horizontally placed loops. Subpapillary venules visible. Capillary pressure 17 to 29 mm Hg.

groups—those with high capillary pressure and those with a low or normal capillary pressure. In the first group the readings ranged between 30 and 75 mm Hg.

It is impossible to classify the patients clinically. Neither the history, the physical examination, nor a study of kidney function reveals any differential features. Similar urinary

ary to hypertension Both schools still have their advocates From the maze of facts and theories that have surrounded the subject, one thesis may be granted as established—that the syndrome of hyperpiesia or essential hypertension may exist without any evidence of nephritis Whether “nephritic hypertension” is a late stage of this or quite a different syndrome is

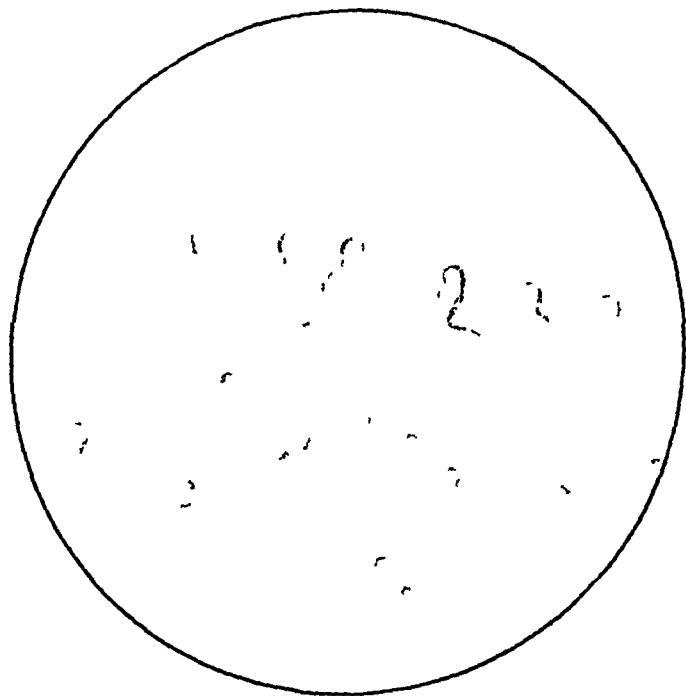


Fig 197—Pulmonary tuberculosis, slight acrocyanosis Venous loop of capillaries dilated Arrangement irregular Capillary pressure 15 to 20 mm Hg

unknown Blood-pressure studies have been singularly unilluminating in clearing up the matter We have learned to appreciate that brachial blood-pressure readings are very variable, and that in many instances they depend on the degree of contraction of the arterioles That the capillaries themselves may be concerned in the maintenance of this pressure was first brought

on appropriate cases, the estimation of the capillary pressure may prove an important aid in the differential diagnosis of glomerulonephritis from other types of kidney disease. It is not, however, of value in the differentiation of nephritic from essential hypertension.

As a rule, in essential hypertension the capillary blood-pressure is low. This may be attributed to a contraction of the arterioles. Any constriction of a vessel raises the pressure central to the obstruction and lowers the pressure peripheral thereto. Thus the view that in essential hypertension there is a constriction of the arterioles is confirmed. Low pressures are found as well in a number of other conditions. In the capillaries of fingers that are clubbed, or in which there is a vasomotor disturbance, as in acrocyanosis, the pressure is low. It is probable, however, that under these circumstances the low pressure is not universal throughout the body, but exists only in the extremities.

It will be seen from this general survey that the capillaries play an important rôle in disorders of the circulation. The study of the significance of capillary disease has just begun, and offers to clinicians as well as to physiologists a fruitful field for future research.

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improbable, however, for change in function to occur without change in structure, but it is conceivable to have such structural changes develop and produce profound disturbances in function without being able to recognize the underlying pathologic changes by our present methods.

In order to deal, then, with the so-called functional diseases we must bend our efforts in two directions. first, to develop methods for the recognition of the characteristic structural change, and second, in the interim we must learn to recognize abnormal physiology, and attempt to develop methods of treatment to modify this abnormal function. As far as the patient is concerned, even in organic diseases, what is disturbing is not the pathologic change, but rather the disturbance in his normal physiology.

I shall present a number of cases this afternoon to demonstrate the rôle of the ductless glands in a few common functional diseases, to indicate the method of establishing the underlying endocrine basis, and to develop a form of therapy based upon such analysis.

The ductless glands play a tremendously important rôle in medicine and the importance of this rôle is constantly being more appreciated. It is unfortunate, however, that the entire subject of endocrinology has been somewhat discredited by the numerous and unwarranted therapeutic claims of highly advertised organic products. But behind the cloud of dust thrown up by these extravagant therapeutic claims many serious workers have made real live contributions to medical progress. What is needed, however, for the progress of this branch of medicine is thorough, painstaking, honest, unbiased study and accurate clinical observation.

Indeed, most of the progress in endocrinology has come largely through accurate clinical observation, and such observation is the most constant factor in medicine. At the present time laboratory methods seem to dominate medical practice, but one can make just as many errors with a test-tube as in clinical observation. Because of the difficulty of clinical study of disturbances of the ductless glands our examinations

gland is a great sensitizer of the autonomic nervous system. It is generally agreed that the autonomic nervous system is an important factor in determining visceral function, and since the thyroid is the great autonomic stimulant the speed of visceral function is to a great extent dependent on thyroid activity. The thyroid also controls the iodine concentration of the blood, and probably has a good deal to do with immunity.

The pituitary gland controls the bony and skeletal growth and development. It plays an important rôle in controlling genital development. It is also an important factor, and possibly initiates various rhythmic functions, and it is, therefore, probably an important factor in such rhythmic functions as menstruation. Chemically, there is evidence to show that it is probably a controller of phosphorus metabolism, and therefore is important in the physiology and development of those organs where phosphorus metabolism is an essential, such as bony growth and cerebral development and physiology. It also has to do with the storing up of sugar and possibly with salt metabolism, and certainly with water metabolism. The rôle of the parathyroids in calcium metabolism is definitely established and they are important in maintaining the acid base equilibrium of the body.

The adrenal glands are necessary and useful organs in normal physiology. They control the somatic changes incident to emotions, they institute the physiologic changes necessary for combat and for emergency responses. Chemically, they probably liberate sugar from the liver for catabolism.

Looking at the various functions broadly, then, we find that essentially the ductless glands are controlling organs, the thyroid controlling speed of function, we might say that the pituitary controls volume, in growth and development, rhythmic and specific metabolic functions, and that the adrenal controls emotional response and emergency response, while the parathyroids probably control the chemistry for nervous activity and maintain tone of the nervous system. The genital organs give character and individuality to function. Apart from their distinctly sexual function they play an important rôle in

I have merely discussed briefly the underlying basis for the understanding of the endocrine factors behind functional disease. In most functional diseases this can be demonstrated, but in others it is not so apparent because of the various factors playing a rôle in functional diseases. For example, in a gastric neurosis with hyperacidity there may be an underlying hyperthyroidism because of the evident excessive autonomic activity. In other diseases this cannot be demonstrated so readily.

There may also be a distinct anatomic basis for the endocrine disturbance in a functional condition, thus a disproportion between the size of the pituitary and the sella turcica which encloses it may give rise to characteristic symptoms.

In the study of functional diseases one must understand the normal physiology of each patient, but this is frequently a variable factor, for there are all sorts of normals. Keith and others have demonstrated that individual and racial characteristics in anatomy, in physiology, and even in psychology, as well as characteristic reactions to diseases, are dependent upon the domination of one or several ductless glands in the physiology of the individual. Thus we have as a normal various types, such as a thyroid dominant type of patient, a pituitary dominant type of patient, a gonadal dominant type of patient, with their combinations. Several combined types can be recognized, such as a pituitary-adrenal type, a thyroid-gonadal type, and a thyroid-adrenal type. While Keith's work has not been generally accepted, the appreciation of some of these individual variations in normal physiology is of tremendous importance in understanding many functional diseases. Practically, however, it is extremely difficult to recognize the combinations, although the simpler types are more easily recognized. In functional diseases each patient reacts in accordance with his individual physiology, and it is therefore essential to understand what each patient's particular normal is.

The value of appreciating the endocrine factors in functional diseases lies especially in the fact that they may give us a guide to therapy, not only to organotherapy, but to other rational means as well. The results obtained in classical forms of thyroid

to the temporal region and to the frontal region, where they remain. They are usually periodic in character, although they may be present all the time. They may appear a day or two before or during menstruation. At any rate, whether they occur only at that time or continually, they are always worse at the menstrual period. These headaches are not infrequently accompanied by fainting spells, or attacks of dizziness, or blurring of vision, and occasionally by polydipsia and polyuria. The headaches are made worse by anything which involves pituitary activity, such as the ingestion of carbohydrates or menstruation. They usually disappear during pregnancy, especially from the fourth month on, but as soon as the child is born the headaches recur.

The examination of the patient always shows evidence of pituitary markings of one kind or another, anatomically, or singular pituitary physiology, and a pituitary psychology. The patients are usually of the Froelich type or acromegalic type, with changes in the secondary sexual characteristics, such as amenorrhea, sterility, etc. The female patients frequently have more or less of a feminine psychology and the males the reverse. In female patients these headaches are frequently associated with dysmenorrhea and in male patients with impotence.

The basis for treatment of pituitary headaches is the fact that physiologic hypertrophy of the pituitary gland in a small sella turcica gives rise to the characteristic headaches, consequently, the feeding of pituitary extract or the injection of pituitrin supplies a substance which removes the need for pituitary hypertrophy, thus relieving the headache. In most instances the results of such therapy are definite, although there are instances in which it is unsuccessful. On theoretic grounds, because the pituitary headaches disappear during pregnancy and because placenta and corpus luteum are the only new elements in the endocrine physiology at that time, they are also used for the relief of pituitary headaches, but in my experience these substances have not been very successful, although an occasional favorable result is obtained.

The burden of proof in all clinical endocrinology is always

ing or in any of the other sensations. She has had two similar attacks since the onset of the trouble.

She had scarlet fever, typhoid fever, measles, and pneumonia as a child, but no other illness.

Her menstrual history began at seventeen. She was always irregular. She would be regular for three months, and since then she has had amenorrhea. When she did menstruate it lasted three days, and the last time it lasted five days. As a rule she bleeds profusely. She had no attacks, no nervousness, no cramps, in fact, she felt fine during the months she menstruated. She is unusually fond of sweets, bread, and potatoes. She drinks a great deal of water at times, and at those times she passes large quantities of urine. She prefers the society of girls to boys. She was very bright at school. Geography and spelling were her best subjects and she does not care for music.

Her father is about forty-eight years of age, living. He is rather short and thin. Her mother is forty-eight years of age, medium stature, though she was stouter formerly. She has two sisters and one brother. One sister is thirteen, the other is eleven years of age. She has a brother of ten. The sister is almost as tall as the patient, but rather thin, and the brother is of medium stature. There is no history of epilepsy, goiter, diabetes, or any other constitutional disease in the family.

Examination —Measurements: Weight, 130 pounds, height, 65 inches, span, 63 inches. Lower extremities, 33 inches, upper extremities, 32 inches, torso, 30 inches. Circumference of head, 23 inches, of neck, 13 inches, of chest, 33 inches, of waist, 28 inches, of buttocks, 37 inches. Pelvis, 11 \times 7½ inches. Pulse, 105. Blood-pressure, 136/70.

The patient is a rather tall, thin, apprehensive, nervous girl. The skin is somewhat dry, scaly, moderately tense. There is no rash, no acne, no tache, no Sergent's line. There are a few pigmented spots above the right breast and on both forearms and one in the left lumbar region. There is a congenital fistula over the sacrum probably leading to a dermoid cyst, surrounded by a streak of long hair extending downward and inward to the anal orifice.

rather narrow There are no areas of tenderness, rigidity, or masses felt

There is a lordosis and scoliosis of the lumbar spine The upper extremities are rather thin The hands are narrow The fingers are long, rather infantile, and there is a slight tremor The lower extremities are thin and show the hairiness above noted



Fig 199—Case I A B Roentgenograph of sella turcica, showing erosion of floor in case of pituitary tumor

Examination of the nervous system is negative except for slightly exaggerated knee-jerks The x-ray examination of the skull shows a large sella turcica with an erosion of the floor and very distinct posterior clinoids, suggesting pressure within the sella turcica

Eye examination by Dr Steinbugler Examination of the eyes shows vision 20/40, and a double optic neuritis more

of the headaches she has a severe pain in the eye with blurring of vision. The headache usually is worse either before or during her menstrual period. Occasionally it comes on after menstruation. It is frequently accompanied by a pain on the top of the head and by dizziness when she stoops over. It usually lasts about a day. She is inclined to be nervous, especially when she works hard, doing her own housework, and she becomes irritable, especially over little things. Her hands perjure moderately. She frequently has indigestion with her headaches. She feels drowsy at times in the afternoon. During pregnancy she is quite free from these headaches and feels better than at any other time. She has no attack at all during pregnancy and she feels very well at that time. She was much stouter as a girl, and about the age of eighteen or twenty years she began to be stout. She is very fond of music. In college she was very fond of mathematics and practical subjects. She is naturally of a calm, even disposition and practically inclined. She has a very even temperament, although she gets depressed occasionally. She frequently feels so nauseated that she vomits, at times her bowels move freely.

She had mumps, measles, scarlet fever, and chickenpox in childhood. She has had an attack of appendicitis and the appendix was removed. A year ago she had an attack of abdominal cramps which was called a stone in the bladder, but the diagnosis was not verified.

She began to menstruate at thirteen. She was very irregular in the beginning. It was always accompanied by severe cramp-like pains and lasted about seven days. She has been married about ten years. Since the birth of her child the menstruation has improved. She has no more pain and she is always regular. The labor was very prolonged. She has no other children.

She drinks a cup of coffee a day, is very fond of bread, which she likes more than anything else, she is not especially fond of meat.

Her father died about sixteen years ago. He suffered with headache, similar to the ones the patient has, but much worse. She takes after her father in everything, and similar headache.

The neck is narrow, somewhat long, the thyroid is palpable, but not enlarged. There is a fulness of the supraclavicular regions, especially posteriorally, which is suggestive of adiposity, but there is no cervical rib. The chest is well developed. The costal angle is acute. The breasts are large and pendulous, with an extensive light areola around the prominent nipples. There is no increase in the mediastinal area of dullness. The lungs and heart are normal.

The abdomen is distended due to a slight tympanites. No areas of tenderness or rigidity present. The liver and spleen are not enlarged. The lower border of the stomach can be made out a fingerbreadth above the level of the navel. The kidneys are not palpable.

Extremities The upper extremities are rather thin. The hands are narrow. The fingers are long and square. The hands are cold and moist, there is no tremor. The lower extremities are rather thin. There is no edema, no hairiness, there is moisture of the skin.

The examination of the urine is normal. The roentgenogram of the sella turcica shows no change in its size or structure. The basal metabolism is +8 per cent. The perimetric reading shows normal visual fields.

This patient is essentially a pituitary dominant type of patient because of the characteristic measurements, the span being less than the height, and the torso greater than the lower extremities, the rather broad features, the primary adiposity, the prominent supra-orbital ridges, the scant menstruation, the history of dysmenorrhea. Psychically she is unemotional, with a practical, matter-of-fact temperament. There was no evidence of any organic disease, the only findings were the constitutional make-up above described, which apparently indicates domination of the pituitary gland in her physiology. She suffers, however, from headaches similar to those of the previous patient who had a pituitary tumor. These headaches are characterized by periodicity by a characteristic pituitary location, by being worse during the menstrual period, by improving during pregnancy. Since her marriage, however, a

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severity of the abdominal cramps she always had to be confined to bed throughout her whole menstrual period. During the time when the headaches are severe she is quite drowsy and feels weak.

She is a nervous type of girl, she does not gain in weight, but at times perspires very profusely. About three years ago before the onset of this illness, she had stomach trouble, characterized principally by abdominal distention, but without definite gastric symptoms. Her bowels were very constipated. She has no falling out of the hair. Her hands perspire easily, but no other parts of her body.

She had pneumonia and measles as a baby. Otherwise the past history was negative. She began to menstruate at thirteen or fourteen years of age and was always regular. Her menstruation is very profuse and lasts eight days. It was always accompanied by the intense headaches above described and severe cramp-like pains. She always has to stay in bed throughout her whole period.

She is very fond of sweets, vegetables, and fruit, she drinks a cup of coffee in the morning and a cup of tea at lunch time. Her father died of appendicitis before she was born and is said to have been tall. Her mother is tall, not unusually stout. She has one brother, thirty-one years of age, who is tall and stout, one sister of twenty-three, taller than the patient, not so stout. There is no history of goiter, diabetes, or other constitutional disease in the family.

Examination—Weight, 82½ pounds, height, 61 inches, span, 60 inches. Lower extremities, 30 inches, torso, 31 inches; pelvis, 9½ x 6½ inches. Blood-pressure, 115/75. Pulse, 72.

The patient is a rather thin, dark complexioned girl. The skin shows no rash, but there is a long streak of light pigment over the lumbar vertebræ. There are two large pigmented spots over the left lumbar region. There is an area of pigmentation over the right knee. There is a pigmented mole over the right lower scapular region. There is a slight evanescent momentary tache. There is no *Sergent's line*. The skin is oily, smooth, and rather tense.

which the x-ray man suggested was a fracture, but apparently it was not a fracture

This patient was suffering from characteristic pituitary headaches. They were periodic in character, they were bitemporal, and were especially severe during menstruation and accompanied by dysmenorrhea. Furthermore, the examination of the patient indicated the pituitary domination in her make-up. This was characterized by the coarse features, by the prominent supra-orbital ridges, the rather broad nose, the wide interdental spacing, the undersize and the characteristic pituitary measurements, the span being less than the height and the length of the torso greater than the length of the lower extremities. The sella turcica was small. There was no adiposity, however, and there were no secondary sex manifestations. The marked pigmentation and the loss in weight, as well as the asthenia, suggest thyroid overactivity, which is probably associative or compensatory.

The patient was put upon pituitary extract, 0.2 gm. three times a day. She returned a week later stating that for the first time her headaches were relieved. Two weeks later she came back stating that she had been through her menstrual period without any headaches and with diminished abdominal cramps during menstruation. She stated she was entirely different and was able to work for the first time during her menstrual period. She was given atropin sulphate, 0.0001 gm., in addition to the pituitary extract for the relief of her dysmenorrhea. This patient was on pituitary feeding for four months. She was free from headaches throughout this time, but she had slight dysmenorrhea at her menstrual period, which was usually relieved by atropin. At this time it was decided to try the effect of placental extract for the relief of the headaches on the theoretic consideration that pituitary headaches are relieved during pregnancy from the time the placenta is fully developed until the birth of the child. And since this is the most important new element in endocrine physiology during pregnancy, the relief of the headaches at this time might be due to a secretion from the placenta. She was put on placental

57½ inches Lower extremities, 28½ inches, torso, 30 inches, pelvis, 10½ x 8 inches Blood-pressure, 115/70 Pulse, 82

The patient is a rather stout, fairly well-developed woman of dark complexion There is no rash on the skin, there is no tache, no Sergeant's line The skin is of olive color, rather soft, velvety, and oily There are no distinct areas of pigmentation

Hair distribution There is an abundant growth of jet black hair on the scalp, with an occasional streak of gray at the temples, with a marked anterior attachment There is considerable hair on the upper lip There is considerable hair over both forearms and legs, over the sacrum, and the pubic hair is feminine The axillary hair is present and the pubic hair has a pyramidal border

The eyes are prominent, the palpebral fissures are normal in width The eyes are dark in color, the pupils are round, equal, and react to light and accommodation Graefe, Stellwag, Mobius, Kocher, and Dalrymple signs are negative The nose is normal, rather broad, straight, with a convex tip The teeth are in poor condition They are crowded together, the upper incisors are rather broad, but twisted The neck is short, the thyroid is not enlarged

The chest is rather broad, the costal angle is wide The breasts are large, pendulous, with large pigmented prominent nipples that secrete milk The lungs and heart are normal

The abdomen is pendulous, with marked inguinal adiposity, and there is diastasis of the rectus muscles The stomach is dilated, the lower border extending about three fingerbreadths below the navel The liver and spleen are not enlarged, the kidneys are not palpable The urine examination is negative

The x-ray of the sella turcica showed a rather long, shallow sella with clubbing of the posterior clinoid and a very long, thin, narrow shelf extending anteriorly The basal metabolism was not done in this case

The patient is suffering with a characteristic pituitary headache She has the physical make-up which indicates a dominant pituitary physiology, namely, the coarse features, the hair over the upper and lower extremities, the adiposity,

67 inches Lower extremities, 31½ inches, torso, 32½ inches Circumference of head, 32½ inches, of neck, 15½ inches, of chest, 35½ inches, of abdomen, 35½ inches, of buttocks, 36½ inches Pulse, 80 Blood-pressure, 105/70

The patient is a rather broad, coarse featured, stout, middle-aged man The skin shows an eczematous rash over the chest There is a slight tache surrounded by a white area, no definite Sergent's line There is no pigmentation, the skin is smooth, soft, rather oily, not tense, with a good deal of subcutaneous fat

Hair distribution The scalp is covered by brown hair, medium anterior attachment, with a bald area extending upward on either side of the temples The eyebrows are long and bushy The beard is rather thick (He shaves twice a week) There is a slight tuft of hair over the ensiform and slight hair over the lower part of the abdomen below the navel The pubic hair, however, is feminine There are some few downy hairs over the forearms and lumbar regions, with extensive hairiness over both legs

The face is broad and coarse, adipose, plethoric, and the skin of the face is oily and coarse The forehead is narrow, rather broad, and receding The nose is straight, with broad, soft tip The eyes are hazel colored There is slight edema of the lower lids The pupils are round, equal, and react to light and accommodation There is no nystagmus Gräfe, Stellwag, Mobius, and Dalrymple signs are all negative The ears are large, the lobules are attached

The teeth The left upper second bicuspid is missing, otherwise they are in good condition, slight pyorrhea in the lower teeth, the upper centrals are broad, with marked interdental spacing, the upper laterals are broad, with similar spacing The lower centrals are also broad, with increased spacing The dental arch is wide, the palatal arch is shallow, with a thick palatal ridge

The throat is congested, the tonsils are absent (not removed), the neck is short and broad, there are no supraclavicular fat pads, the thyroid is palpable, but not enlarged

by Dr A E Jaffin, complaining of headaches of thirteen years' duration

Ever since childhood she remembers having headaches Her mother told her that she would get spells of temporary blindness and dizziness during the attacks of headache She remembers when going to school that she would get headaches during which her vision would become blurred and visions as of flowers would appear But these conditions did not occur during the time of the headache The headaches were mild in character until about thirteen years ago, when they became very severe Since then they have grown very much worse

The headaches begin over the glabella of the nose, extend over the frontal region of the skull, over the top of the head to the left temporal region, where they remain They are periodic and occur during the day or night, usually preceded by visions of flowers, and at times by temporary, momentary blindness They last for a day and she feels very much exhausted following the headaches She passes urine very frequently during the headaches, although she is not unusually thirsty at that time When the illness began the headaches would occur every month, but recently their frequency has gradually increased from every two weeks to every ten days, and now she gets attacks almost every day and they are much more severe She has grown very much stouter The only time when her headaches disappear is during pregnancy, usually from the time when she begins to feel life to the termination of the pregnancy, when the headaches return immediately

From the beginning of pregnancy until she feels life she usually feels much worse The headaches are more frequent and more severe She feels drowsy She vomits continually, she has no appetite and she loses in weight, but when she begins to feel life she is entirely well She is free from headaches and is energetic, also appears to be younger

About a year ago she was constantly drowsy and would remain in bed practically all the time She never perspires, but suffers from heart-burn and a peculiar burning sensation in the ears

the oldest brother is forty, tall, and of the same stature as the patient. The younger brother is about three years younger than the patient, is very big and muscular, the oldest sister is forty-six, suffers from rheumatism, but has no headaches.

Examination—Weight, 188½ pounds, height, 61 inches, span, 58 inches. Lower extremities, 27½ inches, torso, 33½ inches, pelvis, 12 x 9½ inches. Pulse, 86. Blood-pressure, 115/70.

The patient is a rather stout woman, of middle age. She has a marked adiposity in the epigastrium and in the lower inguinal region of the abdomen. Her features are large and broad and acromegalic in type. No rash on the skin other than an occasional acne spot over the back. There is an area of pigmentation over the chest anteriorly and posteriorly, outlining the border of a bathing suit and is probably due to sunburn. Her skin is smooth and soft, not tense.

Hair distribution. The scalp is covered by abundant hair, mostly dark in color, but with occasional gray streaks. The eyebrows are thin, slight hair in front of the ears. There is marked absence of hair over the forearms and legs. The pubic hair is of the feminine type. The axillary hair is marked.

The face shows slight asymmetry, the right side being more evident than the left, and there is a slight weakness of the left side of the face which the patient says she has only noticed this summer. The forehead is broad, the supra-orbital regions are not prominent, the glabella is wide, the eyelashes are long. There is no edema of the eyelids. There is no exophthalmos. The palpebral fissures are of medium width, there is no nystagmus. The pupils react to light and accommodation. Gräfe, Stellwag, Kocher, Mobius, and Dalrymple signs are negative. The ears are rather flat, somewhat congested, oily, and the lobes are attached. The examination of the auditory canal shows a normal tympanic membrane. The nose is rather broad, short, soft tip, the intranasal examination shows no evidence of pathology.

Teeth. The upper front and left incisors are absent, the right upper lateral incisor is large and normal, the canines are blunt. The lower teeth are in good condition.

pituitary in type it was decided to try organotherapy before attacking the sinus trouble. In this case there was such a distinct history of relief during pregnancy that it was suggested to try placental extract in large doses first. The patient was put on about 20 grains of placental extract a day for about a month, with absolutely no relief of the headaches. Placental extract was then stopped and she was placed on whole gland pituitary extract in gradually increasing doses until she was getting from 20 to 30 grains pituitary extract a day, but up to the present there has been no improvement in her condition.

It would seem likely, therefore, that attention to the cloudy frontal sinus might solve the difficulty. She has, however, had her headaches practically all her life. They were definitely associated with fainting spells, with blurring of vision, fatigability, etc., which seem to indicate rather that they are pituitary in character than due to the sinus trouble. There are any number of possible explanations as to why therapy has so far been futile in this case. One is that there may be actual structural changes in the pituitary or that there may be an organic lesion, in spite of the fact that there are no eye symptoms. However, further explanations would merely be mental gymnastics. The fact remains that here was a case who in spite of the very definite pituitary findings and history has not responded so far to rational therapy on that basis.

Note—The sugar tolerance was not done in any of these cases because nearly all of them had a characteristic obesity of the pituitary type. The sugar tolerance test in pituitary diseases is only of value in the absence of characteristic obesity, because it determines a mild degree of increased sugar tolerance which is not present to the extent of causing a characteristic obesity.

ADRENAL CORTEX THERAPY IN HYPERTHYROIDISM

The fundamental basis for organotherapy is a deficiency in the functional activity of one of the ductless glands. If we can recognize such a deficiency and if we have a proper preparation of the deficient gland, the administration of such a sub-

patient's effort to overcome this infection or merely as evidence of disturbance in the endocrine system as a whole in which there is a deficiency in one or several of the other ductless glands.

The gradually accumulating evidence of endocrine physiology indicates that the endocrine system functionates as a system. When one of the glands is injured or its function eliminated or diminished, there usually develops evidence of overactivity of some other glands as well as a synergistic underactivity of different glands.

Consequently, in any condition of overactivity we must solve the problem in two ways: first, we must look for an etiologic factor such as an infection for instance, and, second, we must look for evidence of functional deficiency of some other ductless glands.

This afternoon I shall present a number of cases which demonstrate clinical evidence of deficiency of other ductless glands especially the adrenals in hyperthyroidism. Clinically it can frequently be appreciated that the hyperthyroidism is merely evidence of the patient's response to some etiologic factor such as an infection. Every once in a while a definite focal infection* in the teeth and tonsils is responsible for the hyperthyroidism and a removal of these primary lesions causes a prompt improvement in the symptoms. This is not as common as one expects from the literature, however.

If we are to make any progress in organotherapy in cases of hyperthyroidism, our efforts should be devoted to the discovery of evidence of deficiency in other ductless glands, and to obtain proper preparations of these glands to administer on the basis of substitution therapy. Osler has always emphasized the importance of asthenia and profound weakness as an important symptom in exophthalmic goiter and hyperthyroidism. Kocher has laid stress upon the frequency with which pigmentation and asthenia occur in exophthalmic goiter and hyperthyroidism. Furthermore, he has stated that the feeding of suprarenal extract causes the disappearance of the hyperthyroidism in the patient. Julius Bauer has made similar observations. G. A. Friedman in a recent article, has also

The objective symptoms disappear before subjective improvement takes place. The first notable effect is a gain in weight and a lessening of the asthenia. This is followed by a slowing in pulse-rate, a diminution of the nervousness, and a reduction in blood-pressure, and by a reduction in the basal metabolic rate. In some instances simultaneously and in others later the subjective symptoms have improved. We have also used this substance in cases of gastric neuroses characterized by hyperthyroidism as indicated by the clinical evidence and by the basal metabolic rate.

I do not mean to indicate that this form of therapy is the only therapy for hyperthyroidism, but it seems to me that progress along this line will ultimately develop a specific for hyperthyroidism.

The improvement in our cases has been especially noteworthy, as the treatment has been used principally on ambulatory patients without the use of any other remedies.

Case I. Exophthalmic Goiter—E. R. A young married woman of thirty-six came under observation on March 22, 1921, complaining chiefly of nervousness, palpitation of the heart, and enlargement of the thyroid gland.

She was perfectly well until about a year ago. At that time she noticed an enlargement of the thyroid gland. This was associated with palpitation of the heart and with extreme nervousness. For the last eight months she has noticed a gradually increasing bulging of the eyes. She has pains in the knees, the shoulders, and the lumbar spine. She has shortness of breath on exertion and develops precordial pain at that time. She has lost about 20 pounds in weight. She has occasional burning pain immediately after eating, with an occasional nausea, but no vomiting. Her bowels are constipated. She has profound asthenia and gets tired so easily that she is unable to do her housework. She has occipital headache, but the headache is not characteristically of the pituitary type. She perspires very freely.

She had influenza in childhood. She had no measles, but

the ensiform is not palpable. The breasts are large and well developed. The lungs are normal, the heart is not enlarged, there are no murmurs, but it is rapid. The pulse is 128 and the blood-pressure is 175/95.

The abdomen is not distended. There are no areas of tenderness or rigidity. There are no abnormal masses to be felt. The liver and spleen are not enlarged. The kidneys are not palpable. The lower border of the stomach extends to the level of the iliac crests. The upper extremities are thin. The hands are narrow, the fingers are long, the hands are moist. The lower extremities show nothing abnormal. The urine examination was normal. The roentgenogram of the sella turcica showed no changes. The basal metabolism showed +62½ per cent.

This patient was a classical hyperthyroidism. There was no evidence of any focal infection in her tonsils or teeth. She was placed on adrenal cortex, 0.06 gm three times a day, and was kept on that steadily, gradually increasing to 0.12 gm three times a day. She began to improve about four weeks after the first observation, gaining at the rate of about 2 pounds a month for the first three months, and then about a pound a month, and her nervousness cleared up.

In October, 1921 she weighed 134 pounds. Her blood-pressure was 160/100 and her pulse was 118. The dose of the adrenal cortex was now increased.

In December, 1921 her blood-pressure was 140, her weight was 139 pounds, her pulse was 112. The exophthalmos had practically disappeared.

On January 24, 1922 her weight was 140 pounds, her pulse 104, her blood-pressure 124/96, her thyroid measured 15 inches, and she is entirely free from symptoms.

Her basal metabolism is now +16 per cent.

Case II Hyperthyroidism C. B. A married woman in thirty-nine years of age came under observation in October, 1921. She complained chiefly of enlargement of the thyroid gland, nervousness, and palpitation of the heart. For the last six weeks has noticed enlargement of the thyroid gland. She has grown quite nervous. The illness began with a sudden

are round, equal, and they react to light and accommodation. There is no nystagmus.

The teeth are in poor condition, markedly pigmented, with carious condition in the upper front teeth and pyorrhea. The tonsils are large. The circumference of the neck is $14\frac{1}{2}$ inches. The chest is rather narrow, breasts are of moderate size and well developed, rather pendulous, the lungs and heart are normal except for the tachycardia noted. The abdomen is soft and flabby. There are no areas of tenderness or rigidity present, the liver and spleen are not enlarged, the kidneys not palpable. The abdominal wall is flabby. The upper extremities are thin, the hands are moist, and there is a fine tremor of both hands. The lower extremities are thin and show nothing abnormal. The urine examination was negative. The roentgenogram of the sella turcica was normal. The basal metabolism showed +55 per cent.

This patient was a clinical case of hyperthyroidism which evidently came on in a woman with a dominant thyroid physiology. She was always thin, she was always nervous. She was very active sexually and very prolific. The sudden shock of the injury of her child was what probably initiated the thyroid overactivity. Hyperthyroidism and exophthalmic goiter are extremely common among patients who are considered as thyroid dominant type. In other words, the slightest mental shock or infection reacts upon their thyroid, producing the hyperthyroidism.

She was placed upon adrenal cortex, 0.06 gm. three times a day, to test the value of the remedy before attempting to put her teeth in condition. She came in a month later, stating that her nervousness was very much better, the exophthalmos had gradually diminished, her pulse was 120, and the blood-pressure was 104/75. She weighed 107 pounds.

She did not return until the early part of January, 1922. She now weighs 112 pounds, her pulse varies between 70 and 80, and her blood-pressure is now 135/60. The neck circumference is 11 inches. Her basal metabolism is +23 per cent.

are very thin and highly nervous. There is no goiter, diabetes, or other constitutional disease in the family.

Examination—Weight, 124 pounds, height, 62½ inches, span, 62 inches. Lower extremities, 33½ inches, torso, 29 inches, pelvis, 11½ x 8 inches. Blood-pressure, 145/95. Pulse 122.

The patient is a fairly well-developed, rather tall, thin, highly nervous, and apprehensive young woman. Her skin is soft, oily, rather dry. There is marked pigmentation over the chest, back, and over the abdomen.

Hair distribution. The scalp is covered by long, fine, straight, silky hair, with marked anterior attachment. The eyebrows are rather thick, with a few hairs over the glabella. There are a few scant hairs over the forearms and marked absence over the legs. The pubic hair is feminine.

The forehead is narrow, straight. The nose is long, rather thin, with a soft tip. There is a moderate exophthalmos. The Graefe, Stellwag, and Mobius signs are positive. The eyes are brown, the pupils are round, equal, and react to light and accommodation. The ears are flat, the lobes unattached. The teeth. The upper set are gone and have been replaced by a complete false set, the lower show marked pigmentation, but no purulent secretion, the tonsils are enlarged. The neck is long, the thyroid is moderately enlarged, the circumference is 14½ inches.

The chest is rather narrow, the breasts are small with prominent nipples, with extensive pigmentation. The lungs are normal, the heart is rapid, the rate is 122.

The abdominal wall is pendulous. There are no masses, no rigidity, there is marked tenderness on pressure in the epigastrium. The right kidney is movable. The extremities. The upper extremities are thin, narrow, the hands are moist showing a fine tremor. The lower extremities show marked varicose veins, no edema. Vaginal examination shows a cystocele and rectocele, with slight laceration of the cervix. The urine examination was normal. The analysis of the gastric contents showed a free acidity of 62. The basal metabolism showed +48 per cent.

ago she had enlargement of the thyroid gland, but it disappeared after massage

Examination —Weight, 143 pounds, height, 68½ inches, span, 68 inches Lower extremities, 36 inches, torso, 32½ inches Blood-pressure, 175/90 Pulse, 138

The patient is a rather tall, thin young man The skin is smooth, rather tense, with marked absence of subcutaneous fat There is a definite tache, but a suggestive Sergeant's line There is light lanugo-like hair over the upper lip and on the side of both cheeks There is a slight growth of hair over the thighs and legs and slightly over the forearms and abdomen The pubic hair is of the feminine type The scalp is covered with abundant thick, dark, curly hair, which is attached with a medium anterior attachment The forehead is broad, straight, the eyebrows are not unusually thick The palpebral orifice is of medium width The eyes are brown, the pupils are round, small, equal, and react to light and accommodation The nose is straight, with a soft tip The upper front incisors are replaced by bridgework The lower set is in good condition The canines are long and the upper lateral incisors are narrow The x-ray of the teeth showed a slight apical absorption of the second bicuspid The dental arch is of medium width and the palatal arch is high The throat is congested, the tonsils are slightly enlarged The neck is long, the thyroid is not enlarged, but palpable There is no supraclavicular adiposity The chest is of medium width, the costal angle is a right angle The ensiform is not palpable, the lungs are normal, the heart is not enlarged, there is marked tachycardia, and a slight accentuation of the second aortic sound

The abdomen is not distended There is slight tenderness on pressure in the epigastrium The lower border of the stomach extends to about a fingerbreadth below the level of the navel The liver and spleen are not enlarged The kidneys are not palpable The pelvis is very broad (11 x 7½ inches) The genitals are normal The extremities show slight cyanosis of the hands, which are moist There is a marked fine tremor of both hands The lower extremities show no edema, and only the hairiness

Basal metabolism +15 per cent. Feels much better and stronger

This patient is a young boy suffering from hypertension. There was no evidence of any cardiac, vascular, or renal disease. It was therefore considered as a case of essential hypertension. Because of the tachycardia, the tremors, the nervousness, and the increased metabolic rate hyperthyroidism was believed to be the basic cause. On this basis he was treated with adrenal cortex, beginning with 0.06 gm and increasing up to 0.2 or 0.25 gm taken repeatedly, with the result that there was a gradual reduction in the hypertension with an improvement in the hyperthyroidism. An interesting point worthy of note in this case was the presence of the feminine pubic hair and very broad pelvis in his constitutional make-up. This is worth noting to determine whether the feminine constitutional make-up has anything to do with the greater frequency of hyperthyroidism in females than in males.

This patient was observed for quite a long time, but we must be guarded in drawing conclusions. It is quite likely that the therapy had nothing to do with the improvement of his condition. This may have been due to the adjustment of the basic emotional factors in his life quite apart from the therapy. At any rate, the associated hyperthyroidism was improved. Extensive investigations along this line are being carried out in our clinic.

disease possesses certain distinguishing features. I shall not enter into a discussion of all of these now, they have been amply discussed in the contribution to which I have already referred. It is important to remember that it occurs in relatively young individuals and is not at all uncommon in children. It is presumably of unknown origin, and it bears no definite relationship to infectious diseases. Three facts stand out prominently in respect to its etiology: (1) Its incidence is greatest among the poor, (2) it occasionally develops in the course of or after a pregnancy, and (3) it occurs in association with hypothyroid states. Whether the causative agency has a common basis in all of these is not certain. Its incidence among the poor suggests its relationship to defective nutrition, whereas its occurrence in association with pregnancy and hypothyroid states places its etiology in the realm of endocrine disorders. There is much evidence to support these suppositions, and we shall consider them in the discussion of our cases.

The lack of definite knowledge of the pathology of chronic nephrosis has added to the existing confusion concerning this disease. If we may place the pathologic processes in two categories, (1) general or systemic and (2) local or renal, we may clarify the situation considerably.

Of the general systemic conditions which characterize this disease the most important ones are the changes in the blood, the edema, the albuminuria, and the change in the basal metabolism. The changes in the blood are characteristic of this disease and consist in an increase in the lipid content of the blood, in a decrease of the protein of the blood serum, and in the alteration or inversion of the normal albumin-globulin ratio. Normally the cholesterol content of the blood varies from about 0.175 to 0.225 per cent. Although slight variations occur in other diseases, the most marked increase occurs in chronic nephrosis. In my cases I have found figures varying from 0.300 to 1.300 per cent. I consider this increase of fundamental importance. This increase has since been noted by other observers, and the fact that the serum of certain nephritics may give a milky appearance has been observed by the older writers on nephritis.

by the experimental production of edema by protein under-nutrition

The edema is general and may be very marked. Effusion occurs in all serous cavities. The edema of the face gives in the adult a peculiar grayish-white appearance to the skin, in the child the skin assumes a bluish-white hue, like that of dilute milk, although the examination of the blood does not show any or only a very slight anemia.

You have noticed that I have classified the albuminuria under the heading of general systemic conditions. Albumin in the urine has been the one symptom considered as indicative of renal disease. With the increase in knowledge concerning the disease under discussion it has become more and more evident that the albuminuria of chronic nephrosis is not of a purely local or renal origin, but is the result of a profound general metabolic change. I shall return to this question later.

The one other important change that I mentioned above is the decrease in basal metabolism. I have noticed long ago the close resemblance of this disease to certain mild forms of myxedema and also the beneficial effect of thyroid administration thereon. Dr Lande and myself³ have carried out a series of studies in basal metabolism in cases of chronic nephrosis, these form the subject of another report. We have found invariably a decrease in the basal metabolism, at times as much as 30 per cent below normal. I am convinced that there are borderline cases, on the one side of which there are the cases of chronic nephrosis and on the other side cases of hypothyroidism and fruste forms of myxedema.

As I have stated before, the renal pathology of this disease is still not fully settled. Those who have had occasion to study the kidneys of such cases (Fahr, Munk) give the following description. The kidney is enlarged, soft, smooth, and of a yellowish-white color. The capsule strips easily. On the cut surface the cortex and medulla contrast sharply, the cortex has a yellowish-white appearance and small yellowish-gray dots may be visible. Microscopically there are found changes in the primary convoluted tubules. Fatty degeneration is the

the urine is enormous, just as is often the loss of sugar in diabetes mellitus. How shall we explain the loss? The answer that the kidney cells become permeable to protein is a very hypothetical one, has never been substantiated, and does not add anything to our understanding of the disease. My conception of the albuminuria is that it is the result of an *active excretion* of serum protein by the kidney. Because of the change in the protein (chemical, physical, or biologic), as a result of which the body is unable to utilize it for whatever function the protein serves, it is excreted by the kidney as a foreign substance, just as the kidney excretes any other foreign substance injected into the blood-stream. The change implied is a qualitative one,* although adequate means are still lacking to determine its nature. The quantitative changes in the serum protein which we do find are the result of the drain on the blood-serum caused by the albuminuria.

We are here, therefore, face to face with a condition which is really a general metabolic disorder. The term "nephrosis" is misleading in so far as it puts all the blame on the kidney, which is only of secondary importance in this disease. Proper terminology adds to the clarity of our conceptions. Just as in diabetes mellitus we have a glycosuria and back of this a perversion in carbohydrate metabolism, so in this disease we have an albuminuria and back of this a perversion in protein metabolism. It would be far more appropriate to designate this disease as a "diabetes albuminuricus."

The importance of the conception outlined above is at once evident when we come to the treatment of this disease. Our objective here is threefold: (1) To replace as much as

* The chemical methods of analysis are as yet too crude to determine the fine changes that take place in the blood serum in response to various causes. That such changes do occur is certain. This fact is amply illustrated by the various immunochemical changes which result from infectious diseases and different immunologic processes. Another excellent illustration of the above conceptions is furnished by the comparison of blood sera of different origins. Chemically the blood serum of one species of animal may be exactly like that of another, yet when introduced into the blood stream of the second species may produce very striking toxic phenomena.

admitted to the Pediatric Department on November 20, 1921,* with the chief complaint of inability to pass urine for the last few days and swelling of the body for the last six weeks

Family History—This is of no importance

Previous Diseases—He was born at term, labor was normal, was breast fed for one year Three years ago had whooping-cough During the last year has had measles, chickenpox, and pneumonia He has had frequent attacks of tonsillitis and coughs on frequent occasions He had an attack similar to the present one six months ago, which cleared up in eight days There is no history of scarlet fever

Present Illness—This began about six weeks ago with rapid swelling of the whole body, including face and eyes He had been under treatment at home with no effect During the last two days he passed practically no urine, the small quantity obtained being red and turbid He has vomited twice

Physical Examination—The appearance at the time of admission was that of a child of his age, markedly edematous and of a bluish-white pallor Face and eyelids were swollen, as well as the genitals and lower extremities The lungs showed dulness and diminished breathing over both bases The heart was negative The abdomen was protuberant and a fluid wave could be obtained The blood-pressure was 100 systolic and 80 diastolic

The blood count showed 4,960,000 red cells and 88 per cent hemoglobin The white cell count was 18,400, with 74 per cent. polymorphonuclear leukocytes, 21 per cent lymphocytes, and 5 per cent monocytes The urine obtained on the following days showed a large quantity of albumin with numerous granular casts and was of a high specific gravity

The blood chemistry at the start was as follows

Urea nitrogen	19.6	mgm per 100 c c
Total serum protein	4.2	per cent
Cholesterol	0.628	"

* I am presenting this case by courtesy of Dr H Heimann, Chief of the Pediatric Department

no doubt that his improvement is due to the high protein diet

The above case illustrates the effect of high protein feeding only. The next case will show you that sometimes the protein diet alone does not accomplish the same result, and the addition of thyroid therapy is necessary.

A L., fourteen years of age (Case 204,353), she has been subject to frequent attacks of tonsillitis. A tonsillectomy was performed one year ago. Scarlet fever six years ago, so far as can be determined there was no complicating renal factor at the time. For the six months prior to entrance to the hospital there had been gradually increasing edema, dyspnea, frequency, and nocturia. On admission the physical examination was noteworthy only for generalized edema. The urine contained large amounts of albumin, hyaline and granular casts. The blood-pressure was 125/70. The blood chemistry

Urea nitrogen	19.6	mgm	per 100 c.c.
Inorg. nitrogen	40.3	"	"
Uric acid	2.8	"	"
Creatinin	1.8	"	"
Cholesterol	6904	per cent	

The basal metabolism was -18 per cent.

On admission a diagnosis of chronic diffuse nephritis was made. The patient was put first on the Karell diet, then successively on a carbohydrate and high protein diet, but with apparently little benefit. A salt-free diet and diuretics (diuretin) reduced the edema somewhat, and the weight fell from 106 to 97 pounds, but no further removal of fluid could be effected and the case remained stationary. Then, two months after entrance a high protein diet was again instituted, and, in addition, small doses of thyroid extract were given. Within two weeks the edema had entirely disappeared and the weight had dropped to 85 pounds.

Here we have a case in which the high protein diet had apparently produced no effect until thyroid therapy was instituted. It is quite possible that the failure of the diet at the

of myxedema The urine contained a heavy trace of albumin with many hyaline and granular casts

The blood chemistry was as follows

Urea nitrogen	18.2	mgm	per 100 c c
Incoag nitrogen	37.6	"	"
Uric acid	2.5	"	"
Creatinin	1.9	"	"
Cholesterol	1350	per cent	

The basal metabolism was 20.1 calories, —19 per cent

In view of the findings the patient was put on thyroid extract. Marked improvement of all symptoms followed. The basal metabolism returned to normal, the blood cholesterol diminished and the loss of 23 pounds in weight in four weeks was noted.

We have here a case which on first admission presented all the classical characteristics of nephrosis, and was markedly improved on a high protein diet. The patient came back four and a quarter years later with all the symptoms of myxedema, and was promptly relieved by the administration of thyroid extract. This patient's present condition, subjectively and objectively, depends entirely on whether or not thyroid extract is given. In this circumstance we find the basic difference between the cases of chronic nephrosis which respond to thyroid therapy and those of true myxedema. In the latter the thyroid therapy must be continued indefinitely, whereas in chronic nephrosis the requirement for thyroid is only temporary in some instances only as long as the edema lasts, in others, until the albuminuria is entirely eliminated.

The cases which I have presented to you here are illustrative of the immediate clinical course which chronic nephrosis ("diabetes albuminuricus") pursues ordinarily and the result which follows under the therapeutic management suggested. Inasmuch as my chief object in the present discussion is to throw more definite light on the nature of the malady in question, I have purposely avoided discussing the different complications that may arise, and which alter the course and therapeutic indications.

ment It is classic appendicitis proper and its treatment is unqualifiedly surgical The clinical syndrome is a medical commonplace The patient comes down suddenly with general abdominal cramps, nausea, and vomiting, soon there is fever* and, before long, localization of pain, tenderness, and rigidity to the right lower abdomen The condition is correctly diagnosed by the first doctor to see the case, commonly by the patient himself, and is, as a rule, promptly and properly handled This type needs no further exposition

Type II Pain and Tenderness in the Right Lower Quadrant Without Rigidity or Fever in Asthenic Individuals—This condition is not appendicitis, as such, and surgery is not indicated The subjects of this type are invariably of the asthenic habitus, with slim bodies, long, low-placed viscera, and loose peritoneal attachments Very commonly, indeed, such persons complain of a dull, dragging, or sticking discomfort in the right lower quadrant, and examination reveals tenderness on pressure and at times a palpable and even freely movable cecum In order to interpret such findings correctly it may be helpful at this point to review briefly certain elementary physiologic and embryologic considerations Let us take up first the clinical significance of painful abdominal sensations in general Such sensations may be considered as falling into three distinct (though not necessarily mutually exclusive) divisions †

1 Spontaneous pain due to colic This is purely subjective in its origin, it is intermittent in occurrence, it is, as a rule, relieved by pressure and by the application of heat, and it is caused by increased intravisceral tension anywhere in the hollow organs, as in ordinary intestinal peristalsis, in pylorospasm,

* Comment by Dr A O Whipple, Professor of Surgery, Columbia University "It may be misleading to emphasize the question of fever in acute appendicitis, for we see constant cases of the worst type that have practically no temperature, and in this hospital (Presbyterian) we disregard altogether the question of temperature in the diagnosis Of course, many cases come with acute appendicitis and have a temperature, but it is usually the result of abscess formation, and may not be present at all in the fulminating type"

† Cutaneous hyperesthesia (Herd zones) is too superficial to be confused with the deep-seated pains about to be mentioned

Of further interest in this connection is the rôle played by defective embryonic development. The congenital visceroptotic invalid is, as is well known, a veritable storehouse of embryonic misadventures in morphology. In the region of the right lower quadrant such defects are represented by abnormalities in descent and fixation of the cecum in the direction either of deficiency or excess. Thus, we find the freely movable cecum, the low fixed cecum, the more or less peritonealized cecum covered by thinner or denser "veils" or "membranes," and so on. Though believed by Jackson to be the result of chronic inflammatory processes, the preponderance of opinion, surgical (Mayo) as well as anatomic (Harvey), is in favor of the essential embryonic nature of these enveloping tissues. Recent Roentgen studies (Payne and Trahar) also point in the same direction.

Occasionally the membranes just referred to may cause intestinal obstruction of varying degree. In such rare cases surgery is of course indicated, but even here the danger of further "adhesions" is to be kept in mind. In all other individuals of this type surgery should be the very last resort, for it is axiomatic that asthenics, and particularly neurotic asthenics, are notoriously poor subjects for operative interference.

The treatment of so-called appendicitis of Type II, then, is entirely conservative. Measures directed toward relief of the ptosis and atony—such as abdominal support, rest, fattening, sedatives, etc.—are bound to give results that are satisfactory in proportion to the skill and persistence with which these recommendations are carried out. Fortunately such principles are being gradually acknowledged and the story of "feeling worse after my appendix was removed" is being less and less often heard in consulting room and clinic.

Case I—Persistent pain after appendicectomy, *asthenia achylia gastrica*. Trained nurse thirty-one, single. Comes for examination complaining of continual pain around appendix scar. History reveals long-standing invalidism, many acute infections, tonsillitis, endocarditis, nephritis, etc. Twelve years ago vomiting intense, non-localizing abdominal pain, fever,

side Persistent local soreness Comfortable in the morning, but worse again after several hours' duty

Physical examination reveals extreme asthenic habitus with malnutrition Patient 46 pounds underweight for age and height Tenderness over appendix scar Relief from support of lower abdomen Test-meal shows achylia gastrica (achlorhydria)

Roentgen examination shows marked gastrocoloptosis with atony (see accompanying roentgenogram, Fig 200) No delay in evacuation of stomach Fixation and tenderness in ileocecal region

Comment—The operation in this case was unnecessary The "adhesions" about the cecum were probably congenital Adequate preoperative study should have caused recognition of asthenic habitus and of achylia gastrica The diarrheas and abdominal symptoms were undoubtedly gastrogenous in origin The proper therapeutic indications in this case are, obviously, relief of the ptosis and atony, and administration of hydrochloric acid

Case II—Adhesions following appendicectomy, persistence of symptoms, relief from routine medical management (Note This case was reported last year See The General Management of Functional Digestive Disorders, Med Clin N Amer, 1921 (March), 4, 1550) Railroad brakeman, twenty-eight, married In the spring of 1917 began to suffer from pain in the lower right abdomen, constant, and radiating to the pit of the stomach There were no colics, vomiting, or fever Constipation was severe, the bowels often not moving for a week at a time The condition was diagnosed by his doctor as "intestinal indigestion" Medical treatment for two months brought no relief Operation was performed in June, 1917, for "chronic appendicitis" In four weeks there was return of all previous symptoms Two x-ray examinations were made, and the patient was told that he had "adhesions at the hepatic flexure and gas in the colon" A second operation, performed in June, 1919, revealed a band strangling the small intestine Four weeks after the division of this band there was again

recovered from the fasting stomach (hypersecretion) Test-meal revealed distinct hyperacidity



Fig 201—Illustrating condition in Case III. Film taken forty-eight hours after barium meal, one stool, reclining position. Note low (fixed) cecum despite relative emptying, also low (fixed) midtransverse colon. Appendix visible (arrow)

Roentgen examination showed a low, hyperactive stomach of good tonus, emptying within six hours. The duodenum was normal. The colon filled well but emptied slowly, moderate residues being present at ninety-six hours despite three stools.

resembles, in miniature, that of obstructing distal colon carcinoma, with the difference that in the case under discussion we are dealing with long-standing, benign factors such as spastic constipation, redundancy of the pelvic colon, some forms of colitis (both mucous and inflammatory), and anorectal conditions, such as dyschezia and spasm, whether idiopathic or secondary to local disease (fissure, ulcer, piles). Any such obstruction to the fecal column, particularly when its action is intermittent or recurrent, tends to throw back the contents to the head of the colon (exaggerated antiperistalsis), and thus brings on the usual sequence of hypertrophy and dilatation, with local irritation and subjective discomfort.

In taking the history of such individuals one should not be misled by the patient's bare statement that the bowels move daily or even several times daily. Often, specific inquiry as to the size, bulk, formation, and consistency of the stools is necessary to unmask a true, spastic constipation. It is well to bear in mind that the normal adult stool is composed of one or more homogeneous, soft, sausage-like segments, each at least the thickness of a thumb, and representing in length a total of 10 to 12 inches, which is approximately the extent of the lower gut (pelvic colon and rectum) ordinarily evacuated in the normal act of defecation. Any undue thinness of the excrement (pencil stool) or increased hardness or fragmentation (marble or sheep dung stool) is strongly suggestive of a spastic condition in the lower colon, rectum, or anus. Likewise, one should not overlook the essentially similar nature of what look like normal segments, but what are really conglomerate masses composed of small marbles originating in a spastic descending colon and packed together in the ampulla of the rectum*. Finally, suspicion should attach to a history of repeated small, formed stools—to be distinguished from frequent loose evacuations, i. e., diarrhea—for such defecation in instalments is also suggestive of spasticity.

* For an interesting theory expressing an opposite viewpoint see Burnett, who holds that such "mosaics" consist of fecal units and are indicative of a "normal intestinal rate."

duced to the point of spasm, and direct applications are made "to the contracted area by means of cotton applicators soaked in a saturated solution of magnesium sulfate. When the contractures are above the reach of the sigmoidoscopic tube a soft catheter is introduced through the instrument and 1 to 2 ounces of the solution are injected. In moderate contractures six to eight treatments usually suffice to overcome the spasticity and permit the restoration of normal colonic function. Severe cases may require a larger number of treatments spaced over a period of two to three months' time. The same treatment is efficacious in spastic contractures of the rectum. It must be noted, however, that the magnesium sulfate solution has no effect whatsoever upon sphincter spasm of the anal canal. The indications for treatment of sphincter spasm are direct instrumental dilatations and appropriate treatment of the accompanying lesions of the mucosa."

The writer has used this method with satisfaction. As a rule each treatment seems to be followed by an increase in the size and bulk of the stools and by greater freedom of evacuation. A wider use of this method is to be recommended.

Case IV—Palpable tender cecum diagnosed tuberculosis or chronic appendicitis, spastic colon, anal sphincter spasm due to hemorrhoids and proctitis. Lawyer, twenty-six, married, came under observation October 23, 1921, complaining of a "lump" in the right lower quadrant, weakness, and recent diarrhea. In the past the bowels had always moved daily, but the patient never could take an enema because he had trouble both in introducing the tip and in expelling the fluid. Three years ago he experienced a sudden attack of general abdominal discomfort at night partly relieved by enema. No localization of pain at that time. About two years ago he had "influenza" with much gas distress and constipation. Four months ago there was an attack of pleurisy and discovery of a healed apical tuberculous lesion. Two months ago an attack of diarrhea lasting one week with much tenesmus and gas distress. At this time the patient palpated his own cecum, describing it as a lump the size of a watch in the lower right side. There

Physical examination, October 24, 1921, showed a small, asthenic subject, 28 pounds underweight. Pulse and temperature normal. Cecum palpable and tender. No rigidity. Marked relief from support of lower abdomen. Proctoscopy painful. Numerous external hemorrhoids. Tight and inflamed sphincter. Test-meal negative.

Roentgen examination. Stomach and duodenum normal except for hyperperistalsis. No ileal stasis (at nine and a half hours). Colon still faintly outlined at seventy-two hours, despite three stools. The entire colon very spastic (Fig 202), especially from hepatic flexure onward. Distinct rectal spasm observed (in addition to anal spasm noted on physical examination). Appendix filled near the tip at twenty-four and forty-eight hours. The cecum was free and showed no filling defects or increased irritability either by mouth meal or by colon injection. It was tender throughout the examination.

The stool was negative for tubercle bacilli.

Course. Local treatment for rectal condition. Fattening diet, including olive oil, abdominal binder, sedative mixture, one or two magnesium sulfate instillations. At the present writing, more than three months after the first visit, despite the fact that treatment was not very thorough, the patient has practically no distress in the right side, the "lump" has almost completely disappeared, the bowels are moving freely and regularly, and there has been some gain in weight and strength.

Case V—Tender, gurgling cecum, redundant colon. Married woman, twenty-two, came under observation July, 1920, complaining of pains across lower abdomen and of constipation. The constipation dates back to childhood. The average stool interval was three to four days, but sometimes the bowels were not opened for a week. Evacuation was had only by enema. Cathartics generally caused cramps and no stool. There seemed to be no distress from the constipation as such. In 1916 two attacks of epigastric cramps, not relieved by enemas. In 1918 the patient began the use of mineral oil, with the result that she had a formed stool each day. Had dyspepsia of pregnancy (heart-burn) the next year. Since

no relation to meals. Soreness on pressure in lower abdomen. Sense of incomplete evacuation after enemas.

Examination showed a well-built and well-nourished young woman. The abdomen was soft, there was moderate tender-



Fig. 201.—Same case as Fig. 203. Film made after administration of opaque enema. Note great redundancy and looping of distal colon.

ness below, more in the right iliac fossa than in the left. The cecum was gurgling. The Meltzer sign was moderately positive. The test-meal showed a hyperacidity.

Röntgen examination (Figs. 203, 204) revealed a striking

filled at one hundred and twenty hours, despite two small stools during this interval. There was spasticity of the distal large intestine. The ampulla of the rectum was packed with feces.

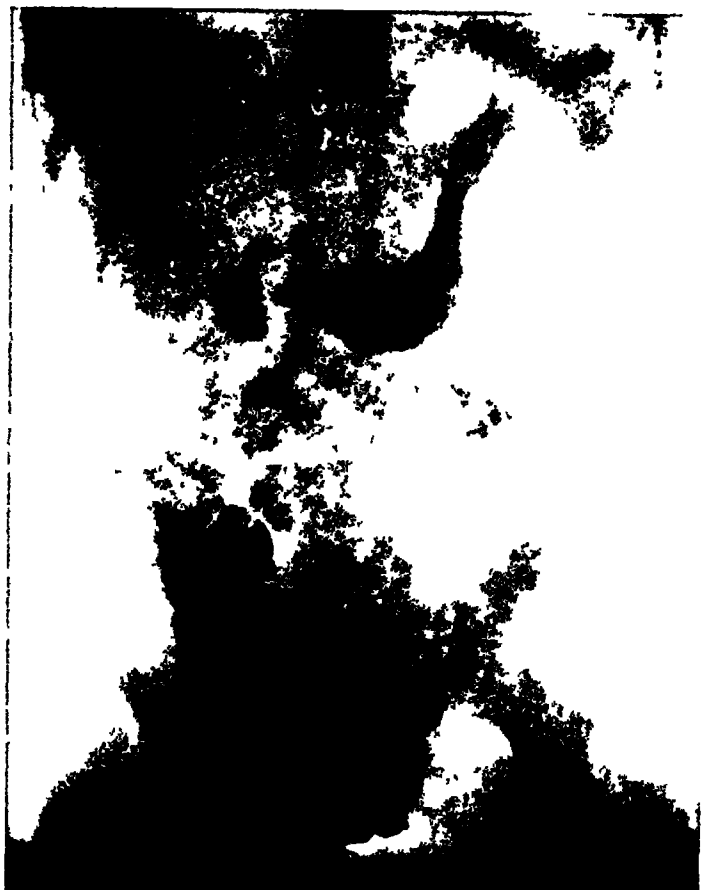


Fig. 205—Illustrating Case VI. Film taken six hours post cibum. Note residue in stomach, also incomplete duodenal cap. The transient gastric retention and duodenal spasticity in this case are reflex phenomena due to dyschezia.

without producing the desire to defecate (classic dyschezia). The cecum was tender, but not fixed, as proved by its gradual elevation on emptying. The appendix was persistently filled.

entire clinical picture might be the result of a reflex from the rectal stasis, particularly as such secondary phenomena as



Fig. 207.—Same case as Fig. 206. Film taken one hundred and twenty hours post cibum. Two small stools in all. Note still further elevation of cecum and appendix (arrow). Also marked spasticity of pelvic colon and large mass in ampulla without provoking the desire to defecate (dyshchezia).

duodenal irritation and pylorospasm are by no means uncommon in children suffering from coprostasis.

woman, twenty-eight, referred by gynecologist to clear up condition in right lower quadrant. For past week the patient has suffered from colicky epigastric distress, also from twitchings in the right iliac fossa, worse on moving about and on pressure



Fig. 209 — Same case as Fig. 208. Note low position of partially emptied cecum at forty-eight hours. Failure to rise when empty means fixation. Compare with Fig. 208. Cecum is probably adherent to cystic right ovary.

No vomiting. Pains are relieved by lying down with hot-water bag. Previous history of diarrhea, but no typical appendix attacks. Long-standing dysmenorrhea. Pelvic examination reveals large cystic right ovary.

Röntgen examination showed normal stomach and duode-

diagnosis lies, of course, between that and a recurrent inflammatory appendicitis. Operative findings are not available at the present writing.



Fig. 210—Illustrating Case VIII. Note low position of cecum at nine hours post cibum. Retrocecal appendix visualized at subsequent examination. Condition probably due to tuberculosis of right adnexa.

Type V. Chronic Irritative Appendicitis.—This is perhaps the most interesting of all the forms of appendicitis. Although the treatment is invariably surgical, the diagnosis may unfor-

In March, 1920 the patient was operated on and an "acute exacerbation of a chronic appendicitis" was found



Fig. 211 —Case of possible chronic irritative appendicitis (not described in text) Note atypical position and wide continuous filling of appendix Film at twenty four hours post cibus

He has just reported (two years after the first observation) that he gained 20 pounds after his operation and feels "fit as a fiddle"

permanent relief after appendicectomy. Married woman, twenty-nine, came under observation in January, 1921. Past history negative. Six years ago onset of vomiting, belching, and general abdominal pain bearing no relation to meals. After nine months the vomiting and belching stopped, the pain continued. Four months ago (October, 1920) the vomiting and belching recurred. The vomiting comes on one hour after meals, the ejecta taste sour, this is never blood. No vomiting takes place before meals, on arising, or late at night. The belching takes place one to two hours after meals. There are frequent severe headaches. The bowels are regular, the appetite is fair. The cramps often cause palpitation and dizziness, and the patient has fainted on two occasions. The pains are never severe enough, however, to double the patient up. The pain is more on the right side, is drawing in character, and radiates to the back. There are no urinary symptoms. There is no nervousness. The patient has lost about 8 pounds in weight.

Examination, January, 1921. Abdomen tender in epigastrium and below umbilicus in midline. No appendix tenderness. No organs felt. Free acid 17, total 40.

Therapy. Bromids, valerian, hyoscyamin, bismuth cerium oxalate, atropin, anesthesin were employed without the slightest relief. Lavages were tried every third day with similar results. Electricity was applied intragastrically in the form of galvanism, with relief for just one day. Even cocain and morphin made no impression. The patient was then admitted to a hospital, where an x-ray examination proved negative and the test-meal confirmed the previous findings. Lenhartz diet was instituted, but the vomiting and pain persisted. A neurologist diagnosed "neurasthenia" and suggested that the patient be fed but one meal a day, which she vomited none the less. After three weeks of hospitalization the patient became so prostrated that whereas she had walked into the institution she had to be removed on a stretcher. Duodenal feeding was next attempted, but the tube was not retained. Almost in desperation, the patient submitted to exploratory operation May, 1921. The stomach, gall-bladder and appendix appeared normal. The latter was

might be arrived at. That it is quite in keeping with the teaching that asthenics tend to functional, whereas sthenics tend to organic, digestive diseases, is obvious. In the writer's hands this test has proved of value though it is realized that a limited non-surgical experience may be misleading. There seems to be increasing agreement as to the correctness of the statement (see under Type II) that operation can, generally speaking, be safely deferred in the presence of pain and tenderness in the right iliac fossa when this occurs without fever or rigidity in *asthenic* subjects. The converse may quite possibly be equally true, viz., that the same syndrome in *sthenic* individuals should be regarded as potentially surgical unless proved otherwise. A rational conservatism demands that only the most watchful waiting be practised, and that no such patient should be dismissed from observation unless appropriate investigation (such as that partially outlined under Type III) reveals some definite distal colon condition to account for the "appendix syndrome," and, furthermore, unless this syndrome is promptly relieved by appropriate medical treatment. The following case is sufficiently impressive to warrant citation in support of this proposition.

Case XI—Single man, twenty-eight, taxi overseer, came under observation July 26, 1921, complaining of recent abdominal cramps. The history revealed irregular eating habits for fifteen years, and for five years heart-burn and nervousness. One year ago onset of indefinite abdominal distress with occasional constipation. For the past two months increasing general abdominal cramps fifteen minutes after meals, lasting one-half hour, also increasing "nervousness." For the past three days sticking pains and dragging sensation in the right lower quadrant.

Examination revealed a stocky subject, soft abdomen, no tenderness. The stomach test showed a low free and a normal total acidity with increased mucus. The Roentgen examination indicated gastric hypertonus and hyperperistalsis with normal emptying. The duodenum was negative. The proximal transverse colon was looped and seemed adherent to the ascending. The appendix was not visualized. The temperature was not

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pain in the back, not judged to be a surgical condition, probably lumbago "

On November 2, 1921, this patient was admitted to the medical service of Harlem Hospital. A family history obtained then by the house staff is as follows. Father died of cystitis developing into kidney trouble, mother died of cancer of the stomach. In the previous history it is recorded that until a year ago the patient was a heavy drinker of alcohol. In childhood he had scarlet fever and measles. Twenty years ago he had pneumonia. Three months ago he had a herniotomy. There is no history of venereal disease. The pigmented mole on the left side of his face has been present since childhood.

The present illness is of three months' duration and is attributed to overlifting. His chief complaints are stomach trouble, pain in the lumbar region and in the back, and also a small lump in the back. His stomach trouble has become gradually worse, and consists of a gnawing or sticking pain in the epigastrium that starts usually about half an hour after a meal and radiates to both upper quadrants. Pain lasts up to, and is relieved by, the next meal. There has never been any vomiting. No black stools have been noticed by the patient. He says a bowel movement sometimes relieves the pain. Pain in the small of the back has been noticed for some time. The pain is a dull ache across the lumbar region, worse on standing up than on sitting down. Occasional pain down the legs accompanies the lumbar pain. The mass in the lumbar region of the spine was never noticed until three weeks ago. The mass gives the patient no pain or any other trouble, though he seems inclined to attribute to it his lumbar pain.

Physical Examination—The patient is an old white man who appears ill.

Pupils react to light and in accommodation, they are equal.
Ears. No discharge or topus.

Nose. No discharge. Mucous membranes are dark red.

Tongue is moist.

Teeth. Many are missing, others show caries and gingivitis.

Throat. No congestion of membranes.

To the left of the midline of the back (Fig 213) at the level of the twelfth dorsal vertebra is a mass about 8 cm square, elevated from the skin 1½ cm, about as dense as contracted muscle. The skin moves freely over it. It is adherent to the deeper parts, from which it seems to arise. There is no constriction at the base. There are large veins about the upper portion. There is an expansile pulsation synchronous with the heart-beat, and a loud bruit, especially marked over the upper portion. There is slight tenderness on firm pressure over the lumbosacral and sacro-iliac joints. There is no tenderness on jarring the spine when the patient comes down on his heels. There is some pain on extending the spine, none on flexing it.

Temperature is 100° F. Pulse is 86. The respirations are 22. Blood-pressure is 125/80 on both sides.

Urine Amber, clear, without macroscopic blood, specific gravity 1020, reaction acid, a trace of albumin, no glucose, a few hyaline casts and a few red blood-cells were present.

White blood count 9200. Polymorphonuclears 72 per cent; transitionals 3 per cent, lymphocytes 25 per cent.

Blood Wassermann was negative on two occasions.

Stools showed no macroscopic or microscopic blood.

On November 17th a lumbar puncture was made. The fluid was clear, without increased pressure. There was no change in the size of the tumor after puncture or change in the pulsation. The Wassermann, the colloidal gold test, the cell count, and the chemistry of this fluid were normal.

The tumor was aspirated on two occasions with fine needles. After passing through a dense membrane, bright red blood was aspirated. This was sent to the laboratory for examination, and when sectioned no tissue other than blood was demonstrated.

An x-ray examination of the spine (Figs 214, 215) shows a rarification of the bodies of the ninth and tenth dorsal vertebra with a projection forward of the anterior wall and a condensation of the margins. The spinous process of the eleventh vertebra is not visualized. The tumor mass is indicated. Compare this with postmortem section of spine (Fig 216).

terized The pain in his back and extremities became so extreme that he was narcotized with morphin constantly A typical



Fig 215—x Ray of the spine (oblique) Note rarification of bodies of ninth, tenth, and eleventh dorsal vertebrae with protrusion of the anterior margin and condensation at the edges of rarifications Note also absence of spinous and transverse processes of twelfth dorsal vertebra, and rarification of eleventh Note normal intervertebral articular surfaces and cartilages

transverse myelitis developed with loss of sensation below the umbilicus and increased for a segment above that The deep

required morphin to procure sleep, although his days were good. An attempt was made to secure fixation of the spine with a plaster-of-Paris jacket. This was unsuccessful, even though a window had been cut for the pulsating tumor. The jacket afforded some support, but did not immobilize the spine sufficiently to abolish pain, and was discarded for a time.

The diagnosis presented considerable difficulty. The outstanding feature of the case was the pulsating tumor. This had to be explained. It could have been either an aneurysm, a cystic tumor to which pulsation was transmitted, or a primary or metastatic pulsating tumor. The systolic murmur at the base of the heart, transmitted to the vessels of the neck, pointed to an aortitis, and suggested a *dissecting aneurysm* of the thoracic or abdominal aorta. In favor of this diagnosis was the man's age, the history of sudden onset after a strain, the pulsating tumor from which arterial blood was aspirated, the apparent erosion of the bodies of the vertebrae without involvement of the cartilages, the presence of blood in the urine, and the onset of paraplegia. The fact that the paraplegia came late, after the pulsating tumor had appeared in the back, was against this interpretation, as it is difficult to understand how the cord and nerves could be spared. The involvement of several vertebrae without uniform distribution of the necrosis was also against this view.

The possible cystic masses which were considered were first an *empyema necessitatis*, or pulsating empyema. Against this was the history of acute onset of pain after a strain without history of pulmonary infection, and the absence of physical signs in the lung, as well as the location of the tumor. Another possible cystic mass was a *cold abscess* of Pott's disease of the spine, with pulsations transmitted from the cerebrospinal canal. Against this was the x-ray picture, which showed no involvement of a joint surface such as is characteristic of tuberculous invasion of the bone, the absence of jar tenderness, and the aspiration of bright red blood from the tumor. Another cystic mass considered was a *spina bifida occulta*. Such tumors communicate with the spinal canal and the lumbar puncture

of a tennis ball, encapsulated, tawny yellow, with areas of necrosis. It was a typical hypernephroma. There was apparently no extension into the veins. The condition of the spine and spinal cord is best understood by referring to the illustration (Fig. 216). A metastatic tumor involved several of the vertebrae, while a fungating mass penetrated the spinal muscles and spread out beyond them as a sessile tumor. The joint

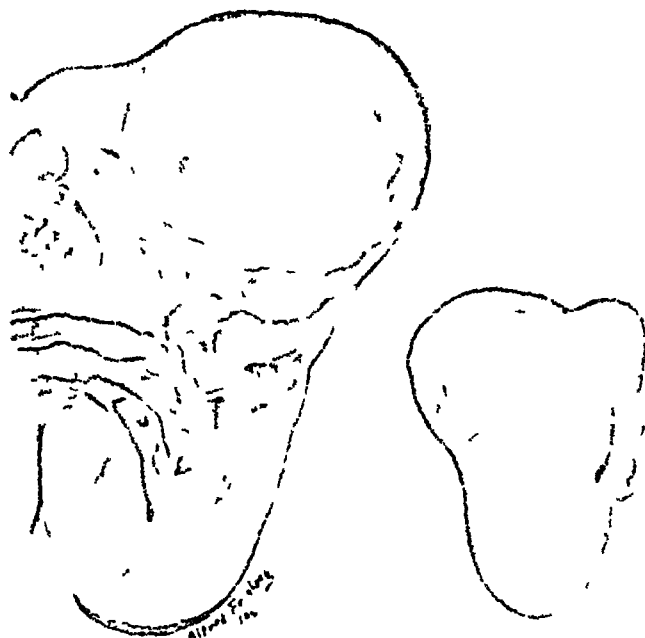


Fig. 217—Left kidney. Note hypernephroma mass with areas of necrosis.

surfaces and cartilages were intact, the margin was lobulated, and showed a distinct capsule.

There were no necrotic areas in the metastasis, which was pink in comparison to the primary growth. The prostate was not enlarged, the gastrointestinal tract was normal. The microscopic examination of the tumor confirmed the diagnosis of gross examination (Figs. 218, 219).

The subject of treatment has not been stressed. If the diagnosis had been made before the metastasis occurred it might have been possible to have excised the tumor successfully. After the metastasis occurred radium might have been employed either superficially or by implantation of radium

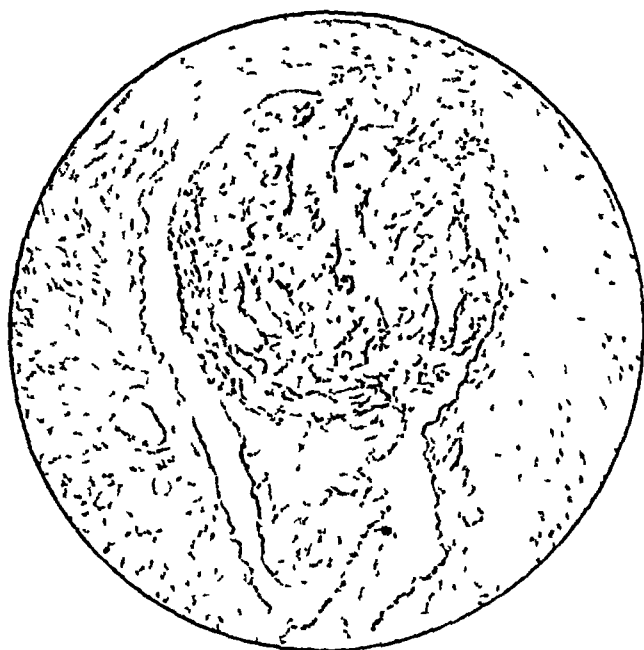


Fig. 219 —High power drawing of metastasis. Note lobular arrangement of cells and marked vascularity of tumor.

emanation in tubes, and x-ray in massive doses might have been applied. In the similar case which has come to my attention the kidney tumor was excised and radium was administered to the bone metastasis in the scapula, yet the patient died shortly after the operation.

roid (Fig 220) The right lobe is larger than the left The thyroid is tender to touch, and when the patient swallows his saliva the thyroid is raised with the trachea, and this evidently causes great pain His heart shows no enlargement, murmur, or

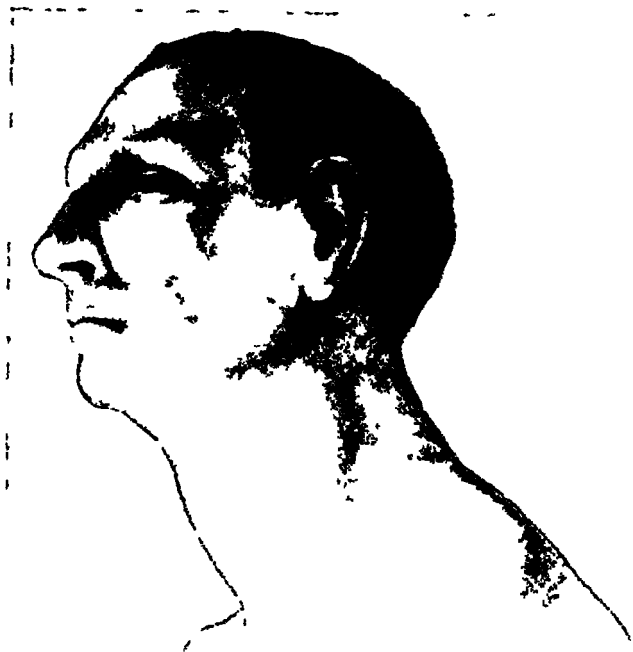


Fig 220—Enlargement of the thyroid in acute thyroiditis

arrhythmia, the sounds are normal The abdomen is normal The liver and spleen are not felt The skin shows no abnormality Excepting the anterior cervical lymph nodes, there is no enlargement There is no tenderness of the bones or joints Reflexes are normal There is no change in sensation other

This patient illustrates a combination of the usual causes of the trouble injury to the neck and a bacterial invasion following exposure

The outstanding features were the difficulty in swallowing and the dysphonia, from which the patient found considerable relief by lying prone with a gauze drain in the mouth so as to remove the saliva, thus obviating the necessity for swallowing. with consequent elevation of the thyroid and the attendant compression between the fasciæ of the neck

Case I—A boy five and one-half years of age was referred to our clinic more than a year ago suffering from asthma. His family history was absolutely negative for any form of protein sensitization. The child had been perfectly well up to six months of age, from that time on he suffered from repeated attacks of coryza, and at the age of one year (after the family moved to Coney Island) he developed his first attack of asthma. He continued to have these attacks, and during the year prior to admission they had become more frequent and more severe. They were invariably preceded by running nose, sneezing, watery eyes, and cough. These prodromata would last for about a day, and at night his asthmatic attack would precipitate, with a gradual subsidence after two to three days. Vomiting and loss of appetite attended all attacks.

The mother insisted that it was something in Coney Island which caused these attacks because the child had never suffered from asthma before they moved there, and whenever she visited with him in Albany or Hudson he was free from attacks. Inasmuch as there was no history of eczema or gastro-intestinal disturbance it was felt that some keratin or animal hair was at the source of this case. The child was then tested repeatedly with all proteins we had on hand (rabbit hair was not one of the stock proteins at that time) and suggestive reactions were given by horse dander, chicken feather, cat hair, and dog hair. Further tests and investigations finally proved them absolutely negative. The child continued to have his attacks, however, and they became more frequent and more severe. But we could do nothing further and this case had to be classified as unsolved.

Several months later the child in one of his severe attacks contracted bronchitis and was advised admission into the hospital. He made a very rapid recovery of both his bronchitis and asthma. Upon the night of his return to his home he promptly developed another severe attack which lasted for three days. A week later I was hurriedly summoned to the child—this was my first home visit. I found the child at the height of a most intense attack, this time with a high tempera-

and has been free from attacks, except once or twice when we have been able to trace them to attempts at desensitization, or contact with bedding containing the rabbit hair.

This case was so impressive that I immediately sent word to three other patients who repeatedly gave negative reactions to the various proteins. To my surprise, all were positive to rabbit hair.

Case II—Boy aged nine and one-half years, who was admitted to the clinic about one year ago suffering from asthma. Family history absolutely negative for protein sensitization. Since his early infancy, the mother states, the child had attacks of what might have been asthma. She used mustard plasters, etc., to relieve him, and as far back as she can remember he has always suffered from coryza and recurrent bronchitis. Mother dates his first real attack at about one year of age. Asthma has been repeatedly diagnosed at different hospitals since then.

Attacks usually started with a dry cough and almost invariably precipitated between 12 and 1 A M., they generally lasted for two to three days, during which time the child would vomit his food and feel generally sick. They occurred perennially, once every week or two. They have, however, become less frequent, now occurring every five or six weeks.

The mother attributed his attacks to eating candy and running around on the street, coming into the house all tired out. However, after going through the gamut of our proteins we could not locate the source of his trouble. After our find in Case No. 1, as I have stated, we tested this boy with rabbit hair, and were rewarded with a positive reaction.

I then questioned the mother about her pillows. She was quite certain that they were filled with goose feathers, and stated that the child had slept on them from birth. But the following day she returned with a bag full of rabbit hair obtained from the pillows. I took some of this hair, had the child breathe it in, and rubbed some into his nose. While he did scratch his nose and sneeze no asthmatic attack ensued. A little disappointed, I took the boy to the animal house, as I had done

were to rub down the rough felt with pumice. Investigation revealed a tremendous amount of finely broken up hairs on his clothing and person. A letter from a Danbury hat factory stated that rabbits' fur was used in the manufacture of practically all felt hats. Dust from the father's factory was extracted and gave a positive skin reaction in this case and all the other cases of rabbit hair hypersensitiveness.

This child, too, was given a rabbit to play with, but developed no reaction until four hours later. It is interesting here to note that this child gave the greatest skin reaction of any of the cases, and showed the slowest clinical response. The attack lasted for two whole days and adrenalin injections gave only temporary relief.

The mother visited the homes in Providence and New Bedford, and returned with rabbit's hair from the pillows. The pillows in the home of the sister where he had been free from attacks, however, contained goose feathers.

The father has been advised to take greatest precautions to remove all the factory dust after a day's work. The child still continues, however, to have occasional attacks which are probably due to the factory dust.

Case IV — A boy of seven and one-half years at the time of admission in whom the same situation prevailed as in the former cases gives the following history. The mother dates the first attack of asthma from eight months of age and from earliest infancy the child has had coryza and bronchitis. He has practically never been free from attacks, and the intervening times between attacks he always suffered from chronic coryza. His attacks also lasted from two to three days and the child also vomits during attacks and suffers loss of appetite.

The search for rabbit hair was very discouraging, but the offending pillow was finally located. He had used this since birth. When it was opened much of the contents floated into the room and the child developed an attack of asthma. A clinical test with a live rabbit resulted similarly to the other cases but this child, in addition, developed large urticarial wheals wherever the hairs rubbed against the face or body.

made of the same fur. The mother noted that the hairs were easily shed, and therefore discarded the coat this winter. A cutaneous test for rabbit hair revealed a positive reaction, and I advised discarding the fur hat.

Case VIII—A child twenty months old, who since infancy has suffered from coryza and recurrent bronchitis, has had about six attacks of asthma this past year, gave a positive skin test to rabbit hair. A visit to the home revealed a large pillow filled with the hair which was used only occasionally. Upon questioning the parents the father recalled that the previous summer when the child played with a rabbit he got a severe attack of asthma. This occurred in the country and the family immediately returned to the city. No importance was attributed to this at the time. The fact that the pillow was used only occasionally accounts for the infrequency of the attacks. I might bring out a further interesting fact: this pillow was given the family by an aunt who has since died of tuberculosis and who had always suffered from asthma.

Discussion—There is a specificity about protein sensitization that commands the respect of all who work in this field, and when a positive skin test is obtained, the physician should leave no stone unturned to locate the offending protein. There was no suggestion given in the histories by the parents of what the cause of the asthma might be, and it was only after having visited the home of Case No. 1 that this type of case was brought to our attention, and there is every indication that many such cases exist, judging from the varied uses that rabbit hair is apparently being put to.

A hair placed on the eyeball or the hair rubbed into a scratch in the skin with or without tenth-normal sodium hydroxide will give a positive reaction. Inhalation of the hair will precipitate an attack the same as exposure to the animal will, so that the diagnosis can be made without difficulty.

While we cannot as yet say anything definitely about our attempts at desensitization, the simple and satisfactory method of treatment is the thorough removal of all the hair.

Walker states "that asthma in infants and very young

considered to indicate that an increased blood-pressure existed during life. This conclusion is correct in the majority of instances. There are some cases of marked cardiac hypertrophy and dilatation that occur in adults and occasionally in children without apparent cause, the so-called idiopathic cardiac hypertrophies, that may for the moment be disregarded.

If we study the relationship of hypertension to nephritis from another angle, that is, during life, instead of at the autopsy table, we find that when the blood-pressure is raised above the normal a nephritis of some sort or degree is almost certainly present. Coupling these two corroborative facts as developed by the clinician, on the one hand, and the pathologist, on the other, it is evident that kidney disease and hypertension are closely related to one another. Thus far our reasoning has been perfectly sound. If in the joy of acquired knowledge we now recklessly assume that every instance of hypertension is secondary to kidney involvement, we are taking unwarranted liberties with the facts at our command. However, this is precisely what has been done, and has led to the belief that an increased blood-pressure is an inevitable sign of Bright's disease, this idea was firmly adhered to until about fifteen years ago, today it is still unduly honored, but not to the same extent.

It is worth while to pause for a moment and take stock of our precise knowledge, clinical and experimental, of the relation of the kidney to blood-pressure. The pivotal idea has always been that a diminished excretory activity of the kidney results in efforts intended to restore normal renal function. Among these changes an increase of arterial pressure is considered to be one of the most important. A great deal of evidence both for and against this theory has been developed.

In animal experiments it has been demonstrated that a reduction of kidney substance results in an increase of blood-pressure (Janeway, Pissler, and Heinke). A total removal of both kidneys, however, does not bring this about. This curious fact has its counterpart in clinical medicine. Prostatic hypertrophy with its attendant, mechanical interference with

consequently their tonicity. The diastolic pressure in such cases must fall below the normal level and the systolic rise, since the blood propelled by the heart meets an unyielding resistance. In former years, before the diastolic blood-pressure was as much studied as it is today, "hardening" of the arteries was considered to be one of the main causes of hypertension. Today we know that very extensive sclerosis of the arteries may exist without very much change in the blood-pressure. This is a matter of clinical observation. These cases are the ones in which the sclerotic process in the blood-vessels has been a primary one. There is another group of patients in which hypertension and thickened arteries occur simultaneously, this is far the more frequent type. In this instance the strain imposed by the increased blood-pressure has brought on the degenerative changes in the arteries. If rigidity of the blood-vessels—arteriosclerosis—lowers the diastolic arterial pressure and raises the systolic but slightly, where are we to seek for the cause of hypertension?

An increased blood-pressure is not a constant phenomenon, as is shown in Figs. 222-224. In these charts it is evident that the degree of variation that occurs is fairly large. This variability of arterial tension furnishes a clue as to the nature of high blood-pressure. There can only be one factor responsible for it under the circumstances, and that is an augmented muscular action on the part of the heart and the blood-vessels. When the tonicity of the arteries is increased the diastolic pressure must rise, for the blood is then held under greater tension than usual throughout the cardiac cycle. It follows, of course, that the systolic pressure increases as well for the heart forces the blood into a reservoir which presents a greater resistance that must be overcome if the circulation is to be maintained. It has frequently been assumed that such a tonic state of the arterial musculature is the sole factor responsible for hypertension, if this were so the diastolic and systolic pressures should vary in constant proportion. This is not the case. The following data taken from a number of patients may furnish evidence to substantiate this statement (Table 1).

We may conclude, therefore, that two factors are concerned in the production of hypertension, the increased force of the heart-beat and the pathologic degree of tonicity in the arteries, and that to a great degree these elements act independently of one another

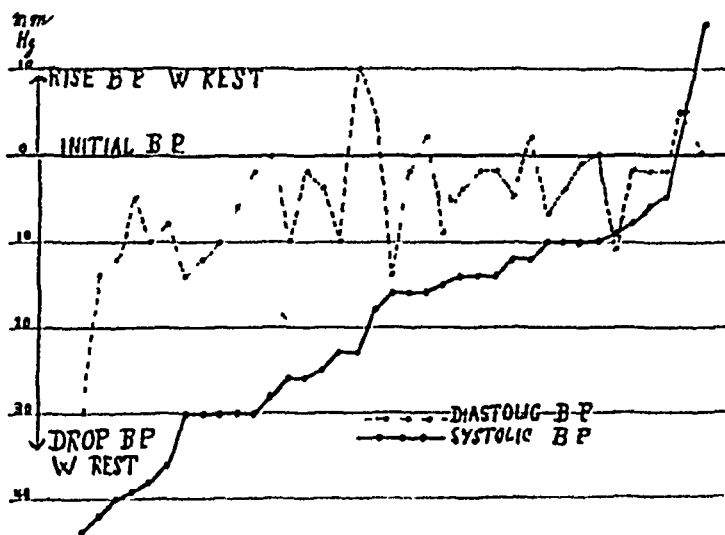


Fig 222—Variation of systolic and diastolic blood pressures from the initial pressure on lying down (short periods of rest) in hypertensive patients (systolic blood pressure of 160 or higher). The horizontal line marked 0 represents the initial pressure. Every vertical pair of dots represents the greatest drop recorded in each case. The distance below the line indicates the amount of drop obtained. The systolic readings of the various cases are connected by a solid line, the diastolic, by a broken line. The observations are charted in the order of degree of drop in the systolic pressure.

The variations are decidedly less in the diastolic than in the systolic pressure. The drop in diastolic pressure, except in the first case, is so slight that it does not appear to be of great clinical significance. This is in marked contrast to the changes that occur in the systolic pressure, which often shows a very great fall on resting.

The Cause of the Increased Heart Action and Tonicity of the Arterioles in Hypertension—It is well established that nervous influences cause the blood-pressure to rise and fall in a most bizarre way. O'Hare and Bois have called attention

affects both the action of the heart and arterioles favorably, and inasmuch as the systolic pressure undergoes the greater improvement it is only fair to surmise that the heart is more readily influenced than the arterioles. All these facts are of great importance in directing the treatment of these cases, and will be taken up a little later.

At this point I wish to accentuate one fact, which may be gleaned particularly from the marked fluctuations in the blood-

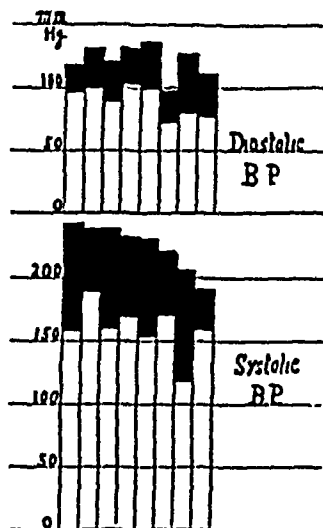


Fig 224 —Drop in blood pressure obtained over a period of several days rest in bed. The columns and their dark areas have the same significance as those in Fig 223. The diminution of blood pressure is much greater with prolonged rest than it is in shorter periods of quiet, as a comparison with Fig 223 shows.

pressure shown in Fig 224. Hypertension is apparently not a compensatory factor that cannot be dispensed with, the patients shown in Fig 224 were as comfortable and as symptomless when the blood-pressure was low as when it was high. Hence the idea, prevalent some years ago, that an increased arterial tension should not be interfered with because it was a compensatory exaggeration of function necessary to maintain the well-being of the individual does not appear to be correct, and

(It is freely acknowledged today that many of the cases that have been diagnosed as uremia are, in reality, due to the changes accompanying cerebral arterio-sclerosis. A study of renal function by more modern methods has revealed this fact. It is probable, therefore, that the above figures should show a higher percentage of deaths due to apoplexy and its results and a lower mortality from uremia.)

It is interesting to note how completely this more modern conception of hypertension differs from the older views in regard to it. Formally an increased blood-pressure was supposed to be secondary to the "small red kidney," now we are certain that the primary contracted kidney develops as the result of a hypertension, and that in most cases a fatal termination does not depend upon the renal involvement but upon the heart.

THE CONTROL OF HYPERTENSION

has been attempted in many ways. None of them have been completely successful, some of them rest upon hearsay and tradition rather than upon clinical observation. Something may be accomplished along these lines in certain cases. However they cannot be treated as a group, but must be studied individually, as the subsequent discussion will attempt to show.

The Effect of Protein in the Diet—For many years protein foods were considered to be at the root of the "blood-pressure evil." The dietary prescription of meat once a day or less and as few eggs as possible has been advocated until the meatless diet has become a popular slogan. There is no doubt about the fact that many of our citizens through an overindulgence in starchy foods are becoming obese and favoring the development of "high blood-pressure" and "hardening of the arteries" by the very diet that is supposed to prevent these maladies.

The feeding of protein, as meats or otherwise, will not tend to increase the blood-pressure of a hypertensive individual. The following case (Table 2) taken from a series of such observations¹ will demonstrate this.

¹ Mosenthal H. O. *Am. J. Med. Sci.* 1920 clx, 893

There is another side to this problem of the relation of blood-pressure to protein food. If the protein constituent of the diet is either curtailed or given in excess over a long period, certain changes are brought about in the body's make-up that entail a lowering or raising of the blood-pressure. Benedict and his collaborators have shown that undernutrition brings about a secondary anemia, diminished vitality, and a lowered arterial tension, it must be borne in mind that the patient pays the price of lessened efficiency if this therapeutic goal is to be reached by these means. The physician must be the judge of how far these two factors may be balanced against each other in each case, and regulate the protein content of the food accordingly.

An increased number of red blood-cells may be accompanied by a rise in blood-pressure. This is true of some cases of polycythemia, but not of all. Why it should occur in some of these patients and not in others has not been determined. However, in certain instances a reduction of the protein food may serve to diminish the red blood-cells and at the same time to lower the blood-pressure. This is a matter that has not been studied sufficiently in clinical medicine, but it may possibly yield favorable results if it is tried out.

The former idea that the retention of the end-products of protein digestion act as irritants that stimulate the heart and the arteries to increased activity and raise the blood-pressure cannot be considered to be correct. Many of these cases do have a high blood-pressure, but its cause must be sought in another direction. Dietetic therapy in these instances demands a lowered protein intake, but while ordering it we must be clear in our mind that we are doing it to relieve the kidney of its burden and not to diminish the hypertension. A case with a high blood chemistry and a normal blood-pressure is the following:

D. K. Age twenty. Blood urea nitrogen 86.2 mg per 100 c.c., blood uric acid 8.3 mg per 100 c.c., and blood creatinin 5 mg per 100 c.c., the urine contained a considerable amount of albumin and a few red blood-cells, the case was evidently a secondary

repeated for the fatty foods. The fats in themselves appear to have no other specific effect upon the level of the blood-pressure.

The Influence of Sodium Chlorid upon Blood-pressure—In 1904 Ambard and Beaujard expressed the belief that salt retention resulted in an increased blood-pressure. Such an inefficient excretion of salt was supposed to be the result of nephritis and renal insufficiency. Various Frenchmen, especially Ambard, confirmed the above theory. Even in the published cases of these authors there is a considerable number that do not exhibit hypertension, furthermore, the very obvious fact has been pointed out that it is generally appreciated that those types of nephritis characterized by salt retention have as their outstanding features albuminuria, edema, and no increase in

TABLE 3

Cases demonstrating the lack of relationship between blood pressure and concentration of sodium chlorid in the blood. These were consecutive cases of hypertension. There are fewer cases exhibiting a sodium chlorid concentration greater than 500 mg. per 100 c.c. than a lower level.

Case	Sodium chlorid mg. per 100 c.c. whole blood	Blood pressure mm. mercury
1	627	226/90
2	588	184/110
3	557	208/94
4	538	221/120
5	519	180/76
6	500	211/136
7	500	200/82
8	500	212/130
9	494	221/120
10	194	224/106
11	488	206/126
12	182	156/100
13	478	216/132
14	478	210/114
15	475	210/116
16	462	246/120
17	450	240/115
18	429	201/128
19	429	170/110
20	429	224/116

of sodium chlorid does not necessarily entail a rise in blood-pressure O Hare's experience in regard to the blood chlorids is very similar to that given above It is as follows

"An interesting sidelight is thrown on the subject by a series of 45 or 46 cases of hypertension These have been arranged according to the height of the maximum blood chlorid About 20 cases or a little under one-half showed normal blood chlorids These normal cases were largely cases of vascular hypertension, whereas those cases showing high blood chlorids were, on the whole, chronic nephritics, with retention of nitrogen bodies as well as salt Curiously enough, those cases that showed the normal chlorids averaged the higher blood-pressure "

Increasing or diminishing the salt in the diet in hypertension is, according to Allen, prone to be followed by a corresponding rise or fall in blood-pressure McLester and Strouse have failed to obtain the same Dr James Short and I, working in this clinic, have not succeeded in affecting arterial tension by the administration of 10 grams of sodium chlorid The detailed description of these observations I wish to reserve for another time The disastrous effect which this amount of sodium chlorid is supposed to have in cases of hypertension we have witnessed only once This was a patient who had a marked renal insufficiency In cases of essential hypertension unaccompanied by renal or other complications it is perfectly safe to administer salt as desired

From the above it appears that sodium chlorid does not affect the blood-pressure, and that no object is attained by putting burdensome restrictions in this regard upon patients suffering with essential hypertension That nephritis of any type may be accompanied by insufficient chlorid elimination must be borne in mind, the salt intake must be adjusted to the ability of the kidney to handle the situation and no attention need be paid to height of the arterial pressure

The Effect of Fluid Intake Upon Blood-pressure—No consideration of the effect of diet on blood-pressure could approximate thoroughness unless this subject were considered Recently

James Short, recently working in our wards was able to confirm O'Hare's results

One incident may serve to show how undue anxiety will increase the blood-pressure. An elderly gentleman, whose life was very methodical and free from almost any unusual interference, was in the habit of visiting me about once a month and have his blood-pressure determined. Over a period of several years it fluctuated between 170 and 190. At one time it reached 240, to return to its accustomed level a few weeks later and remain there. On investigation it developed that the patient's brother had been the subject of an exploratory laparotomy for what the attending surgeon had diagnosed as a carcinoma, the tumor proved to be a benign one and the recovery of the brother seemed assured. With the favorable turn of events the blood-pressure of our patient dropped. *

Occurrences of this sort indicate how vital it is to regulate the business and family cares of hypertensive patients. The difficulty of doing this with any degree of success is fully appreciated and demands an unusual amount of tact, co operation, and forbearance on the part of all concerned.

Rest over shorter or longer periods can be studied more satisfactorily than the intangible effect of nervous influences. O'Hare and Bors have recently done this, and have come to the conclusion, as have others, that relaxation in the recumbent position will diminish arterial tension. A series of cases is presented (Figs 222, 223) which demonstrates the same point.

There are several facts that should be noted if the full significance of these observations is to be taken advantage of. Figure 222 shows how great the drop in blood-pressure may be. A diminution of 10 mm. or more of mercury in the systolic pressure of 3 of the cases is proof of this. On the other hand, the effect upon the diastolic tension is decidedly less marked and ranges within comparatively narrow limits regardless of the fluctuations that occur in the systolic readings. From what was said as to the mode of the production of blood pressure it becomes apparent that such short periods of rest serve to diminish the overactivity of the heart much more than they

effective than the shorter ones. Which method of treatment is to be resorted to depends upon the condition of the heart, the degree of hypertension, and the response of the individual patient to the various forms of treatment.

It must be distinctly understood that the hypertension is not as successfully set aside in all cases as Fig. 221 would indicate. Comparing the blood-pressure observations taken day by day of 2 patients who are now in the ward you will note how in one the arterial tension was done away with while in the other no impression was made upon it by prolonged rest.

TABLE 5

ILLUSTRATING HOW THE BLOOD-PRESSURE WILL DROP WITH REST IN SOME PATIENTS, WHILE IN OTHERS IT DOES NOT

Day of rest	Blood pressure	
	Case 1	Case 2
1	238/134	205/126
2	210/118	185/110
3	218/130	190/100
4	225/138	175/100
5	211/130	165/100
10		120/80

It is, therefore, very necessary to follow the blood pressure by daily observations to determine whether or not the desired effect of relieving the circulatory strain is accomplished.

The Use of Drugs to Control Blood-pressure — The various vasodilators have had their day and have failed to furnish us with a means of permanently reducing hypertension. This is the consensus of opinion at the present time, and I do not believe that these drugs are being used extensively today. Any number of medications may be used to correct symptomatic disturbances, such as constipation, etc., but none of them has a specific therapeutic value. What is true of the vasodilators also applies to the endocrine. It may be that the future holds some medication of value in store for us, but this is a matter to be deter-

is much in the routine therapy of this disease that is traditional and that demands investigation before it can be successfully or conscientiously applied

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The gastric symptoms date back twenty years. From that time, and up to date, he has complained of attacks of epigastric pain, occurring about one week out of every month, occasional intermissions lasting from three to six months were noted. The pains appeared three hours after eating, more marked after the heavier noonday meal, and were burning or cramp-like in character. They were relieved by bicarbonate of soda, not by food. In recent years the pains have been associated with attacks of vomiting, often very severe and prolonged, and occasionally, according to his own description, containing food residue of twenty-four hours or longer. From time to time the vomitus has been streaked with blood, no large hematemesis, however, has been observed.

The appetite is good though the patient is usually afraid to eat for fear of provoking pain. The bowels are regular, urination is normal. There has been only slight loss of weight.

The physical examination reveals a fairly well-nourished man, placid in disposition, a very matter-of-fact personality. If anything, he is hyposensitive to pain with the Libman test of pressure over the styloid process. He is well built, muscular, and shows no signs of malnutrition. The pupils of his eyes are slightly irregular, the right being larger than the left, they react slowly to light and promptly to accommodation. The thoracic examination is negative. He has well-defined tenderness on pressure over the epigastrium and slightly to the right of the median line. Otherwise the abdominal examination is negative except for complete absence of the abdominal reflexes. The knee-jerks and Achilles' tendon reflexes are completely absent. His right radial, biceps, triceps, and periosteal reflexes are active while those on the left are absent. He shows a slightly positive Romberg test. Careful tests for skin sensitivity show scattered areas of hypesthesia over the abdomen and the back. Muscular power on both sides of the body is equal. The blood pressure is 138 systolic, 85 diastolic.

It is known that in September, 1918 his blood Wassermann reaction was negative with the cholesterol antigen and four plus (---+) with the alcoholic antigen. His spinal fluid

curve of gastric acidity rose slowly to a maximum of 74 total and 56 free acidity, was maintained for one and three-quarter hours, and fell slowly to a level of 52 total acidity, at which point it was sustained. At the end of two and three-quarter hours a considerable portion of the oatmeal gruel used as a test substance was still present in the stomach. A normal range of acidity, but a type of curve indicative of a pyloric stenosis or of a pylorospasm, was clearly indicated. Blood was chemically absent from the specimens. A gastro-intestinal radio-

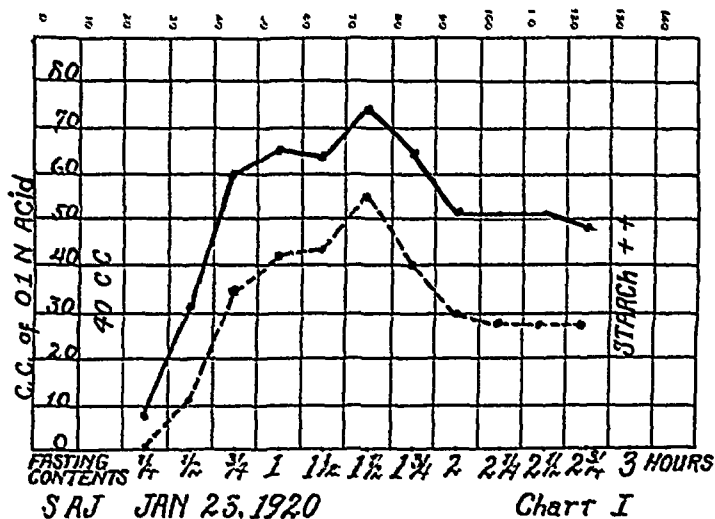


Fig 225

graph made some days later failed to show a lesion, nor was the delayed chemical motility apparent at the six-hour radiographic examination. Such incongruity between the chemical test and the x-ray examination is not very unusual, as a test of motility the former particularly a fractional test-meal, is, when properly interpreted the more reliable. In cases of intragastric lesions associated with intermittent pylorospasm one may be so fortunate on *one* occasion to be able to demonstrate by one test or another a delayed motility. At other times repeated tests may fail to show evidence of delayed motility.

a part of the picture of tabes Irregular contractions have been demonstrated by kymograph as well as roentgenographically, and an occasional case is seen where a spinal lesion causes delayed motility Still it is recognized that the pure tabetic crisis is associated with no definite chemical disturbance of the secretory functions and no constant or clear-cut disturbances in motility Roux has said, "Every tabetic makes his crisis with his own mucosa,"² meaning that individual variations predominate and no class picture is conceivable The pylorospasm and the persistent attacks of food vomiting, therefore, approach that of ulcer,¹ or, at least, that of an intragastric lesion

It was suggested that perhaps the lues had antedated the gastric history and, therefore, that the gastric history could be accounted for on the basis of a gummatous infiltration of the organ Syphilitic ulcer of the stomach is exceedingly rare In this case an ulcer could not be demonstrated with the x-ray Nor is it conceivable that a syphilitic ulcer should persist over twenty years, particularly after three courses of treatment and with a negative Wassermann for many years

The appearance of blood in the vomitus could accompany either an ulcer or tabetic crisis The hematemesis of tabetic crises is usually profuse and occurs at the end of a severe bout of vomiting, the so-called "black vomit," so aptly described by the French, while the bleeding due to an ulcer accompanying the tabetic process is more apt to be smaller in amount and to accompany each individual act of vomiting

The clinical diagnosis of pyloric ulcer complicating tabes was made on the basis suggested, and the patient subjected to a laparotomy At the operation performed by Dr Harold Neuhoef a large indurated peptic ulcer was discovered situated along the lesser curvature and the antrum and posterior wall The base of the ulcer was distinctly felt apparently attached to the face of the pancreas by an inflammatory exudate There was no appearance of large glands and the lesion had all the earmarks of an inflammatory rather than a new-growth process A finger inserted in the pylorus from the duodenal side showed the pylorus markedly constricted

The cases are classified by Lehmann⁴ into One, *true hematemesis accompanying tabes*. These are the cases in which vomiting of blood is an incident or an accident of violent vomiting in the crises. The vomiting of blood under these circumstances is rarely profuse, occurs at the end of the crisis, and only after repeated and protracted bouts of wrenching and vomiting. There are about 15 such cases reported in the literature. Such crises are not infrequently accompanied by the appearance of a large roseola, herpetic or purpuric eruption. In the cases of true hematemesis numerous attempts have been made to explain the phenomenon. Most of them emphasize the so-called "suffusiones hemorrhagiques" of Strauss,⁷ who attributed the hemorrhage to the congestion of the mucosa of the stomach and the violence of the vomiting acts.

Two, a group of cases which includes those in which there is a factor other than the tabes to cause the hematemesis (*false hematemesis of crises*). Such factors may be trauma applied to the abdomen or biliary calculi complicating the crises, but is mainly constituted by cases in which a peptic ulcer or a carcinoma of the stomach occurs with the neurologic phenomena. There are at least 9 true cases of ulcer under these circumstances, practically all of them confirmed at autopsy or operation. One of them is described in American literature by Hitchcock⁸ and was a perforating ulcer of the posterior surface near the lesser curvature. I do not believe that anyone is able to say how many of the other cases of so-called true hematemesis were really cases in which ulcer occurred. In the group of cases wherein an organic lesion complicates the crises the hematemesis is more profound and serious and precedes (often as a melena) or appears irregularly in the course of the crises. The blood may vary in color from wine or bright red to black or coffee-ground color, and varies in amount from 150 to 400 or 500 c c. Exsanguination may occur.

In the ulcer cases erosion of an artery has been demonstrated. Since the publication of my former paper on this subject I have had two oral communications from fellow practitioners in the West, one of a perforated ulcer in the midst

form of violent tabetic crises. The latter is seriously to be considered in the differential diagnosis of such a condition.

The third set of cases classified by Lehmann⁴ includes a group of "Pseudotabes Polyneurotique," by which is meant and described gastric ulcer with symptoms of peripheral polyneuritis, simulating, in clinical respects, tabes. In these cases the Wassermann reaction is negative and the autopsy fails to reveal the degeneration of the posterior and posterolateral group columns characteristic and essential to the diagnosis of true tabes. This is a small group comprising only 6 cases. In all of them a large indurated ulcer was demonstrated, and in many of them degeneration of peripheral nerves, such as the sciatic, has been demonstrated. I have never seen clinically nor have I ever seen described in the American literature cases of this kind. The picture of pseudotabes, that is, a sensory and ataxic disturbance referred to the periphery and not due to a specific luetic infection, we associate in our mind with pernicious anemia or with arsenic- or lead-poisoning, Hodgkin's disease etc. It is hard to understand why such a process should accompany a chronic indurated gastric ulcer. The cases, however, in the French literature have been carefully studied, degeneration has been demonstrated in the sciatic and other peripheral nerves, but not in the lumbar or dorsolumbar levels of a cord. Such a clinical condition could easily simulate true tabes or tabes complicated by ulcer.

In the clinical differentiation there must also be taken into account a form of tabetic dyspepsia which has been described by Roux,² and which is not infrequently seen. Such a dyspepsia, often due to improper diet and often due to the use of drugs, is characterized by pain after meals, eructations, abdominal distention. Such a picture may precede the crises, or may occur independently of crises, and may even be intermingled with attacks similar to gastric crises. It is often difficult to differentiate and to interpret these gastric symptoms. In many of the cases which one sees in every-day practice one has the early signs of locomotor ataxia, and one has indefinite or indeterminate gastric symptoms with or without vomiting.

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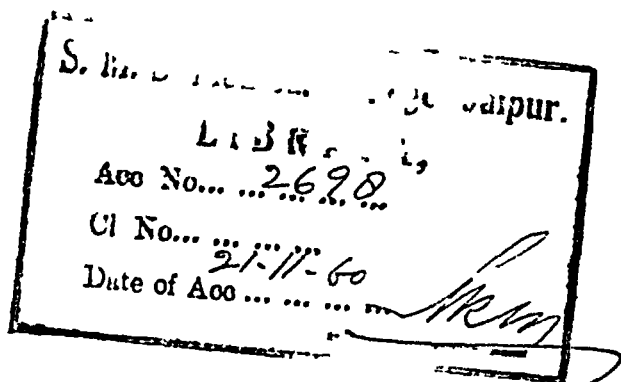
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He has been subject to occasional colds. Following the tonsillitis he had been quite well until last spring, when he had an attack of pain in the epigastrium, with slight nausea and constipation, without fever, headache, or rash. This attack lasted for one or two days. In the summer he had had three such attacks, but had vomited in only one of them. His appetite had been poor during the summer and he had lost 5 pounds in weight. In August, 1921 he was vaccinated with vaccine virus and experienced a rather severe "take." During the latter part of the summer he had had several furuncles over his body.

For some weeks he had been quite well, when, on October 30th, he seemed to feel poorly, complained of slight pain in the epigastrium, and was constipated. His appetite diminished. His temperature was 99° to 100° F. His pulse was slow. On the morning of November 3d he vomited.

Examination on November 3d showed a rather pale, languid boy who evidently when well was quite bright and intelligent, complaining of pain in the epigastrium, which, however, was not very severe. His face was not flushed. The temperature was 99.2° F, the mucous membranes appeared slightly pale. The submaxillary, cervical, and inguinal lymph-nodes were just palpable. The epitrochlear and axillary nodes could not be felt. The skin was smooth and delicate, and there were no eruptions. There were scars of furuncles on the abdomen and back. The lungs were clear to auscultation and percussion. The maximum impulse of the heart was readily localized in the fourth space inside the midclavicular line. The heart was not enlarged. The sounds were clear, regular, and loud. There were no murmurs. The pulse was regular, 90 to the minute.

The abdomen showed slight fulness in the epigastrium, where there was a moderate degree of tenderness. Here the abdominal wall was slightly more tense than elsewhere. There was no rigidity. The lower quadrants of the abdomen were soft and there was no tenderness. In the right costovertebral angle there was very slight tenderness. The edge of the liver was readily palpable in the midclavicular line 3 cm below the costal margin, and there seemed to be some tenderness over it.

On the evening of the 5th, six days after the onset of the acute illness, there was noted a slight icteric tinge to the conjunctivæ and to the skin. On November 6th the boy had improved very markedly. He was taking milk, and though there was still slight nausea and some pain in the epigastrium, it was not nearly so marked as it had been. He was definitely jaundiced. The scleræ had a lemon-yellow tint. The liver remained about the same size. The tenderness over it had decreased. The urine was dark and greenish in color. On the 7th jaundice had increased, but the nausea and epigastric pain had diminished. The urine was amber, clear, 1010, acid, very faint trace of albumin, no sugar, microscopically showed an occasional mucous thread, acetone and diacetic acid were present. The stools were rather light in color, but were not actually clay colored. On November 8th the urine was amber, clear, 1015, acid, very faint trace of albumin, no sugar, microscopically showed occasional white blood-cells, acetone, diacetic acid, and bile were present. By November 9th the jaundice had diminished, his appetite had returned, and he was rapidly improving. The stool was pasty, light grayish-yellow, small amount of residue with some mucus, no blood, ova, or parasites. By November 11th the urine was free from bile, lemon yellow, cloudy, 1018, alkaline, showed no albumin or sugar, microscopically there were occasional white blood-cells and mucous threads, acetone and diacetic acid were still present, though on the 12th the skin and conjunctivæ were still slightly yellow. The liver was readily palpable 3 cm below the costal margin. Convalescence was rapid and he was soon up and about and back at school.

On November 26th he had completely recovered, though there persisted for some weeks a faint yellow tinge to the conjunctivæ. Bile had been absent from the urine since November 10th. His weight was 67½ pounds. The liver was still palpable, but it was not tender. The spleen could be felt with ease on deep breathing coming just below the costal margin.

CASE II—During this boy's illness his sister, aged ten, developed a rhinitis and acute coryza, and for this reason was examined and found otherwise normal. She had always been

epidemics of jaundice occurring at intervals in different parts of the United States, and in this older literature these epidemics are usually referred to as instances of Weil's disease. In 1886 Weil¹ described a form of jaundice occurring in epidemic form which was accompanied by fever and enlargement of the spleen, evidence of nephritis, and which in a fair proportion of cases was fatal. A disease which corresponded to this description was noted subsequently from time to time in various countries and was common in Japan.

In 1914 Inada and Ido, with their associates,² succeeded in transmitting to guinea-pigs the typical experimental disease which in these animals was accompanied by jaundice, hemorrhages, and albuminuria. The transmission was accomplished by inoculating guinea-pigs with the blood of patients suffering with the Japanese form of infectious jaundice. They further discovered in the blood and various organs of the inoculated animals, as well as in the blood and organs of human cases, a new spirochete which they designated *Spirochæta ictero-hæmorrhagiæ*. This organism could be cultivated upon appropriate media, and when inoculated into guinea-pigs gave rise to the same disease that was produced by the inoculation of blood of human cases of Weil's disease. Since the publication of their original work this type of infectious jaundice has been identified by the discovery of the specific organism in various parts of the world, and occurred as one of the serious, though not very common, infections among the English, French, and Italian troops on the western front during the war. An excellent description of the disease is given by Dawson and Hume.³

Further experimental work upon the etiology of infectious jaundice and the transmission of the disease showed that the spirochetes were eliminated in large numbers in the urine, particularly during the later stages of the disease and in convalescence. It is, therefore, discharged over long periods of time from the urinary tract. The observations of Inada, Ido,

¹ *Deut Arch Klin Med*, 1886, xxxiv, 209

² *Jour Exp Med*, 1916, xiii, 377

³ *Quart Jour Med*, 1917, v, 90

lassitude, occasionally vomiting and diarrhea, intense jaundice, epistaxis, hematuria, melena, and hemorrhagic vesicles. There was frequently stupor or delirium. Fever was present in some of the patients, but in others it was absent. The stools were clay colored. The leukocytes varied from 20,000 to 24,000. The urine showed albumin, bile, and casts. At autopsy the icterus was extreme. There was cloudy swelling of the kidneys, the liver frequently presented the appearance which is observed in acute yellow atrophy. In the second group the course was extremely rapid, with jaundice, wild delirium, and rapid death. In this group autopsy frequently disclosed deep areas of necrosis in the gastro-intestinal tract. Eight of these cases were examined during life, with special reference to the presence of spirochetæ. Both the blood and urine were examined microscopically, and, moreover, injected into guinea-pigs. The results were all negative. In 3 of the fatal cases the liver was searched for spirochetæ, but none were found. Through the kindness of Dr Noguchi it was possible to examine the excreta of these 2 cases of mild jaundice to determine whether they contained during the disease or during the convalescence *Spirochetæ icterohæmorrhagæ*. Results from guinea-pig inoculations were entirely negative, and no evidence of the presence of this organism could be discovered by Dr Noguchi in either case.

The type of disease which is described by Symmers is extremely severe, but in many of the epidemics, descriptions of which come to one usually by word of mouth, the course of the disease in children is very mild. Stokes, Ruddeman, and Lemon¹ refer to a moderately mild epidemic type which two years ago was common in Minnesota, and in the autumn of 1921 I happened to see a number of such cases with slight fever and jaundice which occurred at that time in New Haven, Conn. Indeed, reports of cases of jaundice occurring as house or town epidemics are coming from various parts of the state, and it is of interest to quote a note in a recent number of the Journal of the American Medical Association which gives some idea of the prevalence of this disease and the interest that it is creating

¹ Arch. Int. Med., 1920, xxvi, 521.

effort should be made along that line. And we feel reasonably convinced that if we begin to study each group by itself many important facts are bound to be correlated with their respective groups.

Today we wish to consider the clinical and pathologic pictures caused by infection of the endocardium by the *Staphylococcus aureus*. And when we remember that it was less than twenty years ago that a rather heated discussion took place at a meeting of the New York Pathological Society as to whether a *Staphylococcus aureus* found in blood-cultures had any real significance or was merely a contamination, and when we find how little literature there is on the subject, it is not unreasonable to hope for a broadening of the picture through future study, nor unprofitable for you to have your attention directed to it.

We have not time today to discuss these cases from the aspect of *Staphylococcus aureus* infections in general, interesting as that would be. We shall present their case records to you in full, but shall limit the discussion to the cardiac features. We ask you to remember that all 3 of these patients were desperately sick during the period of hospital observation and that, in consequence, there are numerous omissions in their records.

CASE I

(J. H. History 52,010) A young schoolboy, aged thirteen, entered the hospital November 16th, with a history of having fallen upon his right knee five days previously. Since then it had been so painful that he had had difficulty in getting about. On the day before admission he felt chilly and sick and went to bed.

Further questioning developed the fact that in 1919 he had had a furuncle on his forehead and in April, 1921, one on his nose. In addition, he had had a "sore" on the dorsum of his right foot for two weeks preceding his injury, and from this "sore" pus had been expressed on the day before coming to the hospital.

Physical Examination—Temperature, 103° F., pulse, 88,

November 21st Wound shows very little discharge There is evidence of an abscess over or within the thyroid W B C 9800 Polys 88 per cent There are still indefinite signs of pneumonia at the angle of the right scapula Heart unchanged Blood-culture shows hemolytic *Staphylococcus aureus* in both flasks

November 22d Much worse Temperature, 106° F, pulse, 150 W B C 26,400, polys 92 per cent Failed gradually and died that day Urine examinations were negative, but no cultures were made

During his course the temperature was never below 102° F and was irregular between that point and 106° F, while the pulse was between 100 and 150

Autopsy 9176 The body is that of a rather well-developed boy, 162 cm in length There are no cutaneous petechiæ seen The hips are rather narrow The line of the pubic hair is straight. There is no hair in the axillæ, and only a small amount over the thighs and legs There is no superficial glandular enlargement There is a large open wound in the inner side of the right leg, 29 cm in length, extending down to the mesial surface of the tibia from one epiphyseal line to the other The cortex of the bone has been chiseled away on this surface and the cavity of the bone is filled with soft, semisolid, purulent material in the upper part, in the lower part there are reddish-black clots The margins of the wound in the soft parts are covered with a purulent exudate The right knee-joint contains a slight excess of clear fluid The internal and external saphenous veins, also the femoral and tibial veins, are quite free of thrombi The abdominal cavity is negative In the mesentery are found several calcified lymph-glands Each pleural cavity contains a slight excess of turbid fluid The pericardial cavity is negative

The heart weighs 340 grams The epicardium is everywhere smooth and glistening The chambers contain post-mortem clot and are otherwise negative The tricuspid ring measures 12.5 cm in circumference The left leaflet of the valve is quite thin and delicate throughout On the right half of the posterior or septal leaflet there is a delicate fibrinous

The *right lung* weighs 250 grams. There is a delicate fibrinous exudate on the posterior surface of the lower lobe, and also on the lateral surface of the middle lobe. There are numerous subpleural petechiæ seen everywhere over the lower lobe. In the middle lobe is a firm area, which on section is found to be dark red in color. It reaches to the pleura and is quite obviously an infarct. The lower lobe shows numerous areas of bronchopneumonia.

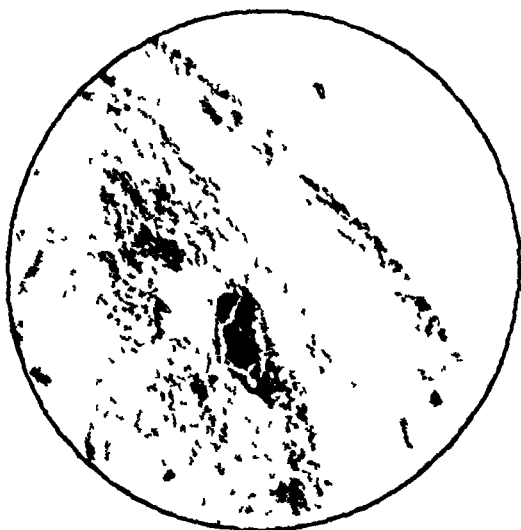


Fig 188—Case 1. *Staphylococcus aureus* endocarditis, tricuspid valve. Masses of bacteria in depths of valve and in exudate upon the surface.

The *left lung* resembles the right in its external appearance. In the lower lobe there are several characteristic infarcts, in one of which there are seen small abscesses.

The *spleen* weighs 230 grams and is rather soft. The pulp is soft, reddish-gray, and opaque.

The *thyroid* is swollen. On section it is found to contain numerous pockets of yellow pus of varying size.

The other organs show nothing abnormal.

Histologically, the sections of chief interest are those of the tricuspid valve, the lungs and the thyroid.

Physical Examination—Temperature, 103 8° F, pulse, 132 respirations, 42 A frail, stuporous, slightly cyanotic boy who was a little irrational and seriously ill Tongue dry and coated Pharynx congested Cervical glands just palpable Some dulness at base of right lung posteriorly with fine râles at both bases Heart overactive, but regular There is a soft systolic murmur at the apex Abdomen negative Spleen not felt No petechiæ Entire left leg from below knee to the hip swollen, hot, and tender W B C 21,200, polys 87 per cent The urine showed a faint trace of albumin and a few leukocytes and red blood-cells No sugar A diagnosis of osteomyelitis of the femur was made, and bearing in mind the previous case, the following additional facts in his history were obtained Last spring and summer he had had several boils, but none lately One month before onset an abscess in his ear had been opened From the description, this was a furuncle in the canal

Operation was performed immediately Osteomyelitis of the femur was found and drained Cultures from this as well as from the blood showed a hemolytic *Staphylococcus aureus*

Course.—November 24th A little better Abdomen tense, but not tender There is a friction-rub over the left border of the precordial region, affected by respiration W B C 15,600, polys 72 per cent

November 25th Rapid, grunting respiration, with marked cyanosis Heart action rapid, but regular There is a systolic murmur at the apex and a friction-rub which seems to be pleuropericardial in nature Lungs clear anteriorly Posteriorly there is dulness, with patchy bronchial voice and breathing over the left lower lobe, and dulness with a friction-rub over the lower half of the right lower lobe W B C 20,200, polys 89 per cent In the evening temperature 106° F, pulse 130, respirations 60 Marked dyspnea and slight cyanosis No petechiæ or skin eruptions No signs of meningeal irritation Ear drums normal

November 26th Slightly better W B C 16,000, polys 93 per cent Blood-culture showed a hemolytic *Staphylococcus aureus* Sweats profusely

leaflet has been destroyed below this thrombus, and posterior to the leaflet there is a large, soft, white, opaque, friable mass filling the space between the leaflet and the septum. Below the aortic leaflet, in the septum membranaceum, there is a perforation about 0.5 cm in greatest diameter. The edges of this opening are covered with fibrin and a probe passes through



Fig. 189—Case 2. *Staphylococcus aureus* endocarditis tricuspid valve

it into the thrombotic mass lying posterior to the tricuspid valve (Fig. 190). In the myocardium of the left ventricle there are two small abscesses. The heart otherwise is negative.

The right pleural cavity does not contain any fluid. The right lung weighs 430 grams. The entire surface of the lower lobe is covered with a thick, fibrinopurulent exudate. The surfaces of the upper and middle lobes are partly covered with

The remaining organs are negative

The section of the femoral vein shows a thrombus adherent to the intima. There is no organization of the thrombus. The wall of the vessel is moderately edematous, and the fat and connective tissue about it also show edema, and are infiltrated chiefly with mononuclear cells.

The section from the muscle along the margin of the incision in the thigh shows great accumulations of polymorphonuclear leukocytes, in which are often large masses of cocci. The muscle-fibers adjacent to these infected foci are in places shrunk to mere threads, in other places they are swollen, hyaline and vacuolated, and the nuclei have disappeared.

The section of the heart shows the abscess in the fat extending down to the underlying muscle, and in the abscess are great masses of cocci. The myocardium adjacent to the abscess is beginning to degenerate.

Tricuspid valve. The section shows upon both surfaces of the valve close to the perforation an accumulation of fibrin and platelets in which are great masses of Gram-positive cocci. The valve beneath a portion of the exudate is entirely necrotic, and as one passes toward the free margin it is seen to be edematous and bacteria are found in the depth of the leaflet. Polymorphonuclear leukocytes are entangled in some parts of the exudate. Still closer to the free border of the valve there is only edema. The mass posterior to the leaflet is made up of platelets, fibrin, red blood-cells, and polymorphonuclears. Scattered throughout are great quantities of Gram-positive cocci.

In the sections of the lung there are found abscesses with great masses of cocci within them. Some of these abscesses appear to have had their origin in infected infarcts. In one of the large branches of the pulmonary artery is an infected thrombus, and the wall of the vessel beneath the thrombus is necrotic. In other sections of the lung there are characteristic infarcts in which are large masses of Gram-positive cocci.

The section of the spleen shows the typical picture of an acute splenic tumor.

Tongue coated and dry Lips cracked Fauces, pharynx, and tonsils reddened On the inner surface of the left cheek there was a small hemorrhagic blotch Neck was stiff, but not retracted The thyroid was not enlarged No lymphatic glands palpable The lungs showed only a few fine râles in right axilla and at both bases

	Space
Heart,	2- 6 cm
At right,	3- 9 "
Sternal,	4-11 "
Margin,	5-12 "

Action regular There was visible pulsation in second left space No thrills Sounds were rather loud There was a soft systolic murmur at the apex, and at the base there was a second systolic murmur, loudest in the second left space, not transmitted upward

Abdomen was symmetric There was resistance to palpation, but no rigidity or tenderness Liver, spleen, and kidneys not felt

The knee-jerks were present, but sluggish No Kernig, Babinski, or clonus Musculature of legs very well developed and firm

The skin about the toes and heels was thickened and caloused and in places reddened The right heel was moderately tender, but there was no swelling and no general redness, although there were some small red spots, 1 to 2 mm in diameter, which were partly erythematous and partly hemorrhagic

On the lower part of the forearms and over the dorsum of the hands were several erythematous patches, 3 to 4 mm in diameter, which did not fade out entirely on pressure

Vaginal examination showed nothing abnormal except a slight, yellowish-green discharge Rectal examination negative

Blood count W B C 11,800, polys 76 per cent No malaria organisms

The diagnosis made on admission was "Septic endocarditis"

Course—September 12th There is slight ulceration of the gums Right ear shows a little redness of upper wall of the canal and the upper margin of the drum

liver, pancreas, kidney, and adrenals, abscesses in heart muscle, pancreas, kidney, and mesentery, infarcts of spleen, kidneys, and mesentery, hemorrhages into skin, pleura, pericardium, heart muscle, esophagus, stomach, pelvis of kidneys, and ureters, bronchopneumonia, acute and chronic pleurisy, hydrothorax and ascites, acute bronchial lymphadenitis, acute splenic tumor, acute embolic nephritis Brain not examined

The organ of special interest in this case is the heart It weighs 280 grams There are numerous petechial hemorrhages beneath the pericardium The foramen ovale is patent The right auricle and ventricle are negative except for a few subepicardial petechiæ The pulmonic and tricuspid valves are negative The mitral valve is not thickened, but there are upon it soft, friable vegetations which extend back from the free margin to the line of closure The chordæ tendinæ are not involved These vegetations are light yellow, they are rather flat and condylomatous-like The largest of the vegetative masses is on the anterior leaflet There are vegetations similar to these on the aortic valve Neither of these valves show ulceration In the myocardium are small hemorrhages and abscesses

The microscopic examination revealed numerous bacterial emboli and abscesses in the myocardium Many of the arteries are completely plugged by masses of bacteria The section of the mitral valve shows that there has been considerable destruction, that there is an acute fibrinopurulent exudate upon the surface, and in the exudate are great masses of cocci An artery near the base of the valve is plugged with a bacterial mass

It is of interest that this case showed an abnormally large thymus, and the individual had the hair distribution of the opposite sex

CLINICAL DISCUSSION

The outstanding fact about these 3 cases is that all suffered from a general septicemia or bacteremia, and that the endocarditis was but an incident, though an important one, in the general picture Now it has been recognized for at least thirty

of the causative organism. In the third place, such study will aid in a better understanding of endocarditis, its mode of origin, and the body's defensive mechanism. The latter is especially important, for it is a well-known fact that only a small proportion of the cases of *Staphylococcus aureus* bacteremia develop endocarditis, 20 per cent in this hospital. Why, in the presence of such a virulent septicemia, do the great majority of heart valves escape? And finally, the ability to determine the presence or absence of such an endocarditis has a very definite bearing upon the prognosis. Thus we know that approximately 75 per cent of cases showing *Staphylococcus aureus* bacteremia die (Libman, Soper). Knowing this, we can immediately tell the patient's friends that he has in general a 25 per cent chance of recovery. But the presence of an endocarditis reduces his chance to zero. And I believe that further study will enable us to pick out the cases of endocarditis among the *Staphylococcus aureus* bacteremias, although we certainly cannot do it with any degree of confidence today.

If we consider these cases from the standpoint of the septicemia, the embolic phenomena, and the cardiac signs, certain points will be brought out which we can verify or disprove in future cases.

Septicemia—We cannot diagnose *Staphylococcus aureus* endocarditis without the knowledge that there is a *Staphylococcus aureus* bacteremia. Naturally we depend upon blood-cultures to settle this point, but this involves a delay of from twenty-four to thirty-six hours, and it dulls our diagnostic wits and our powers of observation to depend entirely upon the laboratory. We should form our surmises, based upon facts, and allow the laboratory to verify or refute them. We need not go into the picture of septicemia. Our cases today have furnished you with it in all its virulence. The point which concerns us is whether there are any means at our disposal, apart from blood-cultures, of determining the etiologic agent. The occurrence of past or present *Staphylococcus aureus* infections is of the utmost importance. Our experience has led us to feel that the history of boils in any case presenting the picture

Another type of skin lesion is the irregular ecchymosis. These lesions were quite definite in a case seen here some time ago. One of the lesions was excised and presented the following microscopic picture: "Section shows a small area with a necrotic center surrounded by an area of marked infiltration with polymorphonuclears. The connective-tissue cells show a marked hyaline degeneration and there is considerable edema. The blood-vessels are filled with red cells, fibrin, and numerous white cells. The skin appears normal. Gram stain shows numerous staphylococci in the necrotic area. They are especially numerous about the blood-vessels, which appear to be plugged by a solid mass of them."

In addition to these lesions, Libman has reported numerous milary abscesses in the hairy scalp.

There may be emboli to almost any part of the body, giving the characteristic signs and resulting in a purulent focus. At least one embolic aneurysm has been reported (Libman). Urine cultures frequently show the *Staphylococcus aureus*.

Abscesses in or beneath the muscles are highly suggestive of this organism.

Cardiac Signs—We have learned previously that non-hemolytic streptococcus endocarditis is almost always engrafted upon a previously damaged heart valve. With the *Staphylococcus aureus* this is not true. None of today's cases showed evidence of an old endocarditis, and this holds true for most of the cases.

Perhaps the most important aid in diagnosis of an endocarditis, once a *Staphylococcus aureus* bacteremia is established, is the development of a new cardiac murmur or an alteration in the quality of an existing murmur. This is especially true for diastolic or presystolic murmurs. It is scarcely necessary to point out the difficulty of differentiating a functional from an organic systolic murmur. It is, therefore, most essential for us to make very careful and repeated examinations of the heart in these cases, noting our findings accurately, for it is *change in the signs* which is generally of greater significance than the *signs themselves*.

The autopsy findings were Abscess of left scapular region, osteomyelitis of left acromium process, Staphylococcus aureus septicemia, acute endocarditis (Staphylococcus aureus), abscesses in heart, lungs, liver, and kidneys, septic spleen, gangrene of left great toe, multiple multiple cutaneous abscesses

The heart in this case showed many small abscesses in the myocardium, especially of the left ventricle and the papillary muscles. On the left cusp of the mitral valve was a small, friable vegetation along the line of closure and extending down on the chordae tendineae. In the tricuspid valve were small petechiae in all the leaflets.

A section of the mitral valve showed an exudate upon the surface in which were numerous Gram-positive cocci. Upon the surface of the tricuspid valve were masses of similar cocci, none, however, were seen in the depths of the valve. The myocardium was extensively involved by abscesses.

The other case in this group was a man, age sixty-five (Autopsy 8357), who was admitted to the hospital on two occasions with a history of nephritis and cardiac decompensation. At the time of his last admission there was an abscess of the left buttock which finally healed completely. Some time later the edema of the extremities and scrotum became very marked, and on two occasions the scrotum was incised, with considerable relief from the edema. A week before his death the whole lower portion of the scrotum became gangrenous. His temperature, which previously had varied between normal and 100° F, gradually rose to 103.5° F.

The findings of interest to us in the autopsy are centered chiefly in the heart, which weighed 770 grams. The right auricle and ventricle and the tricuspid and pulmonic valves were essentially normal. The endocardium of the left auricle was scarred in places. The mitral valve was thickened, and in both leaflets there were hemorrhagic areas, and the surface over these appeared to be somewhat ulcerated. The wall of the left ventricle was increased in thickness. The aortic cusps were moderately sclerotic and stiffened, and the endocardium

Some of these have been described as being reddish gray, others pinkish, and some yellowish white

The necrosis of the valve, it would seem, advanced with actual liquefaction, and may be so extensive that perforation of the leaflet occurs, and the opening in the leaflet may be plugged by the thrombotic mass

Another feature is the tendency for the process to extend to the adjacent myocardium, and abscess formation with discharge of the abscess content into the blood-stream may result either in the formation of a small cavity in the heart wall or, as in one of these cases reported here, in perforation of the septum. These thrombotic masses upon the valves are heavily infected and are another fertile source for infected emboli. The lesions in the myocardium are chiefly abscesses such as are found in other organs

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